

SAMPLE SEARCH INITIATED 09:44:43 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 13 TO ITERATE

100.0% PROCESSED 13 ITERATIONS 6 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 44 TO 476
PROJECTED ANSWERS: 6 TO 266

L2 6 SEA SSS SAM L1

L3 11 L2

=> DIS L3 1- IBIB HITSEQ
YOU HAVE REQUESTED DATA FROM 11 ANSWERS - CONTINUE? Y/(N):Y
THE ESTIMATED COST FOR THIS REQUEST IS 90.09 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:N
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=> DIS L3 1- TI HIT IBIB IABS
YOU HAVE REQUESTED DATA FROM 11 ANSWERS - CONTINUE? Y/(N):Y
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L3 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Enzymatic synthesis of the enantiomers of 2-Amino-2-methyl-4-phosphonobutyric acid
IT 103-80-0, Phenylacetyl chloride 78405-44-4, 2-Amino-2-methyl-4-phosphonobutanoic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(enzymic synthesis of enantiomers of 2-amino-2-methyl-4-phosphonobutyric acid)
ACCESSION NUMBER: 2004:997619 CAPLUS
DOCUMENT NUMBER: 142:240508
TITLE: Enzymatic synthesis of the enantiomers of 2-Amino-2-methyl-4-phosphonobutyric acid
AUTHOR(S): Ragulin, V. V.
CORPORATE SOURCE: Institute of Physiologically Active Compounds, Russian Academy of Sciences, Chernogolovka, Russia
SOURCE: Russian Journal of General Chemistry (Translation of Zhurnal Obshchei Khimii) (2004), 74(8), 1297-1299
CODEN: RJGCEK; ISSN: 1070-3632
PUBLISHER: MAIK Nauka/Interperiodica Publishing
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:240508
ABSTRACT:
Enantiomers of (HO)2P(O)CH2CH2CMe(NH2)CO2H were obtained by penicillinamidase-catalyzed hydrolysis of (HO)2P(O)CH2CH2CMe(NHC(O)CH2Ph)CO2H (1), which favors hydrolysis of the (S)-isomer. The carboxamide 1 was prepared from racemic (HO)2P(O)CH2CH2CMe(NH2)CO2H by N- and O-silylation using (Me3Si)2NH followed by N-acylation using BnC(O)Cl and O-deprotection.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Synthesis of phosphinic acids on the basis of hypophosphites: IV.
Synthesis of pseudo- γ -glutamylglycine and its enantiomers
IT 38056-67-6P 351904-41-1P, DL-[3-Amino-3-(hydroxycarbonyl)propyl][2-(hydroxycabonyl)ethyl]phosphinic acid 352359-46-7P 856766-88-6P
856766-89-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(asym. synthesis of pseudo- γ -glutamylglycine phosphinic acid pseudopeptides via penicillamidase catalyzed hydrolysis)
ACCESSION NUMBER: 2004:997594 CAPLUS
DOCUMENT NUMBER: 143:97611
TITLE: Synthesis of phosphinic acids on the basis of hypophosphites: IV. Synthesis of pseudo- γ -glutamylglycine and its enantiomers
AUTHOR(S): Ragulin, V. V.
CORPORATE SOURCE: Institute of Physiologically Active Compounds, Russian Academy of Sciences, Chernogolovka, Russia
SOURCE: Russian Journal of General Chemistry (Translation of Zhurnal Obshchei Khimii) (2004), 74(8), 1177-1181
CODEN: RJGCEK; ISSN: 1070-3632
PUBLISHER: MAIK Nauka/Interperiodica Publishing
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
A new method for construction of pseudopeptide mols. was proposed, exemplified by the synthesis of DL-[3-amino-3-(hydroxycarbonyl)propyl][2-(hydroxycabonyl)ethyl]phosphinic acid (I) (pseudo- γ -glutamylglycine), starting from ammonium hypophosphite. Enzymic synthesis using immobilized penicillamidase allowed preparation of the enantiomers of I.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Synthesis of a novel class of α,α -disubstituted amino acids: α -alkyl- γ -phosphonoglutamic acids
IT 663943-11-1P 663943-13-3P 663943-15-5P 663943-16-6P
663943-17-7P 663943-19-9P 663943-23-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of α -alkyl- γ -phosphonoglutamic acids)
ACCESSION NUMBER: 2003:509546 CAPLUS
DOCUMENT NUMBER: 140:217969
TITLE: Synthesis of a novel class of α,α -disubstituted amino acids: α -alkyl- γ -phosphonoglutamic acids
AUTHOR(S): Olczak, Jacek; Olma, Anna; Owczarz, Malgorzata; Krawczyk, Henryk; Zabrocki, Janusz
CORPORATE SOURCE: Institute of Organic Chemistry, Technical University of Lodz, Lodz, 90-924, Pol.
SOURCE: Peptides 2000, Proceedings of the European Peptide Symposium, 26th, Montpellier, France, Sept. 10-15, 2000 (2001), Meeting Date 2000, 379-380. Editor(s): Martinez, Jean; Fehrentz, Jean-Alain. Editions EDK: Paris, Fr.
CODEN: 69EDWK; ISBN: 2-84254-048-4
DOCUMENT TYPE: Conference
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:217969
ABSTRACT:
A symposium report. A novel class of glutamic acid analogs containing both

α -substituent and α -phosphono functionality was synthesized via alkylation of α -amino acid derived 2-phenyl-4-alkyl-5(4H)-oxazolones by tri-Et 2-phosphonoacrylate. Subsequent ring opening in acidic conditions releases the α -carboxylic group and allows for all remaining functionalities to be still protected. The phosphono group could be selectively deprotected by means of trimethylsilyl bromide without affecting other functional groups.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
 TI Conservation of the ligand recognition site of metabotropic glutamate receptors during evolution
 IT 56-86-0, L-Glutamic acid, biological studies 2552-55-8, Ibotenic acid 2686-70-6, L-Homocysteine sulfinic acid 3106-85-2 14857-77-3, L-Homocysteic acid 52809-07-1, Quisqualic acid 78405-44-4 85148-82-9, S-4-Carboxy-3-hydroxyphenylglycine 111900-31-3, 1S,3S-ACPD 111900-32-4, 1S,3R-ACPD 117857-93-9, L-CCG-I 146669-29-6, RS- α -Methyl-4-carboxyphenylglycine 147782-19-2, DCG-IV 157141-16-7 169209-63-6 169209-65-8, α -Methyl-4-phosphonophenylglycine 169209-66-9 170984-70-0 170984-72-2 176199-48-7, LY 354740 177188-14-6 279684-29-6D, stereoisomer II
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (metabotropic glutamate receptors ligand-binding site conservation during evolution)

ACCESSION NUMBER: 2000:236781 CAPLUS
 DOCUMENT NUMBER: 133:69122
 TITLE: Conservation of the ligand recognition site of metabotropic glutamate receptors during evolution
 AUTHOR(S): Parmentier, M.-L.; Galvez, T.; Acher, F.; Peyre, B.; Pellicciari, R.; Grau, Y.; Bockaert, J.; Pin, J.-P.
 CORPORATE SOURCE: Centre INSERM-CNRS de Pharmacologie-Endocrinologie, UPR 9023-CNRS, Montpellier, 34094, Fr.
 SOURCE: Neuropharmacology (2000), 39(7), 1119-1131
 CODEN: NEPHBW; ISSN: 0028-3908
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 ABSTRACT:

Mammalian metabotropic glutamate receptors (mGluRs) are classified into 3 groups based on their sequence similarity and ligand recognition selectivity. Recently, we identified a Drosophila mGluR (DmGluAR) which is about equidistant, phylogenetically, from the 3 mGluR groups. However, both the G-protein coupling selectivity and the pharmacol. profile of DmGluAR, as analyzed with mutated G-proteins and a few compds., look similar to those of mammalian group-II mGluRs. In the present study we carefully examined the pharmacol. profile of DmGluAR, and compared it to those of the rat mGlu1a, mGlu2 and mGlu4a receptors, representative of group-I, II and III resp. The pharmacol. profile of DmGluAR was found to be similar to that of mGlu2R, and only very small differences could be identified at the level of their pharmacophore models. These data strongly suggest that the binding sites of these two receptors are similar. To further document this idea, a 3D model of the mGlu2 binding domain was constructed based on the low sequence similarity with periplasmic amino acid binding proteins, and was used to identify the residues that possibly constitute the ligand recognition pocket. Interestingly, this putative binding pocket was found to be very well conserved between DmGluAR and the mammalian group-II receptors. These data indicate that there has been a strong selective pressure during evolution to maintain the ligand recognition selectivity of mGluRs.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

TI Structure-function relationships for analogs of L-2-amino-4-phosphonobutanoic acid on the quisqualic acid-sensitive AP4 receptor of the rat hippocampus

IT 407-41-0, O-Phospho-L-serine 4378-43-2 5652-28-8 13138-33-5
 23052-81-5 73913-63-0, O-Phospho-D-serine 74265-32-0
 78405-44-4 78739-01-2 78944-89-5 79055-67-7 79055-68-8
 79469-41-3 80902-11-0, .dbldag.O-Methylphosphonyl-L-serine 81338-23-0
 81338-24-1 90632-40-9 90632-41-0 103439-17-4 103439-18-5
 116139-40-3 133753-34-1 133753-35-2 143152-37-8 143235-21-6
 143235-22-7 144030-86-4

RL: BIOL (Biological study)

(quisqualic acid-sensitive AP4 receptor binding by, in CA1 hippocampus, structure in relation to)

ACCESSION NUMBER: 1992:584255 CAPLUS

DOCUMENT NUMBER: 117:184255

TITLE: Structure-function relationships for analogs of L-2-amino-4-phosphonobutanoic acid on the quisqualic acid-sensitive AP4 receptor of the rat hippocampus

AUTHOR(S): Schulte, Marvin K.; Whittemore, Edward R.; Koerner, James F.; Johnson, Rodney L.

CORPORATE SOURCE: Med. Sch., Univ. Minnesota, Minneapolis, MN, 55455, USA

SOURCE: Brain Research (1992), 582(2), 291-8

CODEN: BRREAP; ISSN: 0006-8993

DOCUMENT TYPE: Journal

LANGUAGE: English

ABSTRACT:

Hippocampal CA1 pyramidal cell neurons are sensitized to depolarization by L-2-amino-4-phosphonobutanoic acid (L-AP4) following exposure to L-quisqualic acid (QUIS). The authors examined the interaction of 43 structural analogs of L-AP4 with both the 'induction' site and the QUIS-sensitive AP4 site in rat hippocampus. The synthesis of cis- and trans-4-phosphonoxy-L-proline, 3-(RS)-amino-5-phosphonopentanoic acid and 2(RS)-amino-5-phenyl-4(RS)-phosphonopentanoic acid (γ -benzyl AP4) are described. None of the test compds. interact with the induction site; thus L-QUIS remains the only compound known to induce this effect. However, one compound (L-2-amino-3-(5-tetrazolyl)-propanoic acid (L-aspartate tetrazole) 'pre-blocked' and reversed the effects of QUIS. In addition, the potency of 16 analogs increased more than 4-fold following exposure of slices to L-QUIS. Among these, L-AP4, L-AP5, 2-amino-4-(methylphosphino)butanoic acid (AMPB), and E-1(RS)-amino-3(RS)-phosphonocyclopentanecarboxylic acid (E-cyclopentyl AP4) displayed IC50 values of less than 0.100 mM after QUIS. The results presented here suggest that the QUIS-sensitive AP4 site requires a spatial configuration of functional groups similar to that present in E-cyclopentyl AP4. The presence of a primary amino group and a phosphorus-containing group (either monoanionic or dianionic) appear to be required, however, a carboxyl group is essential for interaction. The pharmacol. of the QUIS-sensitive AP4 site suggests that it is distinct from other known binding sites for L-AP4 in the central nervous system.

L3 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

TI Antagonist activity of methyl-substituted analogs of 2-amino-4-phosphonobutanoic acid in the hippocampal slice

AB Four monomethyl-substituted analogs of 2-amino-4-phosphonobutanoic acid (APB) [23052-81-5] an antagonist of excitatory pathways in the central nervous system, were prepared to investigate the steric requirements of the APB receptor. Me groups were incorporated at the amino, α -, β -, and γ -positions. The β - [95742-06-6] and γ -methyl-substituted analog [79469-40-2] of APB were moderately potent antagonists in excitatory synapses to the hippocampal perforant

path, as judged by extracellular recording techniques, whereas the N- [96249-46-6] and α -methyl-substituted analog [78405-44-4] had much lower potencies. All of these APB analogs had very low potencies in the Schaffer collateral pathway. The APB receptors in the perforant path displayed more tolerance of methyl-substitution at the β - and γ -positions of APB than at the amino or α -positions in this system.

IT 78405-44-4 79469-40-2 79469-41-3 95742-06-6

RL: BIOL (Biological study)

(hippocampus synaptic neurotransmission inhibition by, mol. structure in relation to)

ACCESSION NUMBER: 1985:198188 CAPLUS

DOCUMENT NUMBER: 102:198188

TITLE: Antagonist activity of methyl-substituted analogs of 2-amino-4-phosphonobutanoic acid in the hippocampal slice

AUTHOR(S): Crooks, Stephen L.; Freund, Ronald K.; Halsrud, David A.; Koerner, James F.; Johnson, Rodney L.

CORPORATE SOURCE: Coll. Pharm., Univ. Minnesota, Minneapolis, MN, 55455, USA

SOURCE: Brain Research (1985), 329(1-2), 346-9
CODEN: BRREAP; ISSN: 0006-8993

DOCUMENT TYPE: Journal

LANGUAGE: English

ABSTRACT:

Four monomethyl-substituted analogs of 2-amino-4-phosphonobutanoic acid (APB) [23052-81-5] an antagonist of excitatory pathways in the central nervous system, were prepared to investigate the steric requirements of the APB receptor. Me groups were incorporated at the amino, α -, β -, and γ -positions. The β - [95742-06-6] and γ -methyl-substituted analog [79469-40-2] of APB were moderately potent antagonists in excitatory synapses to the hippocampal perforant path, as judged by extracellular recording techniques, whereas the N- [96249-46-6] and α -methyl-substituted analog [78405-44-4] had much lower potencies. All of these APB analogs had very low potencies in the Schaffer collateral pathway. The APB receptors in the perforant path displayed more tolerance of methyl-substitution at the β - and γ -positions of APB than at the amino or α -positions in this system.

L3 ANSWER:7 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

TI Displacement of DL-[3H]-2-amino-4-phosphonobutanoic acid ([3H]APB) binding with methyl-substituted APB analogs and glutamate agonists

AB The binding of DL-2-amino-4-phosphonobutanoic acid (I) [20263-07-4] to rat brain synaptic membranes was saturable (K_d = 6.0 μ M; B_{max} = 380 pmol/mg/protein), Ca^{2+} - and Cl^- -dependent, and diminished upon freezing the membrane preparation. The L-isomer of I [23052-81-5], L-glutamic acid [56-86-0], and L-aspartic acid [56-84-8] were more potent as displacers of I binding than the resp. D-isomers. With the exception of kynurenic acid [492-27-3], all the other compds. examined (L- and D-glutamic acid [6893-26-1], L-glutamate tetrazole [65914-80-9], D-2-amino-5-phosphonopentanoic acid [79055-68-8], 2(RS)-amino-2-methyl-4-phosphonobutenoic acid [78405-44-4], DL-2-amino-4-(methylphosphino)butenoic acid [53369-07-6], 2(RS)-amino-3(RS)-methyl-4-phosphonobutanoic acid [95742-06-6], and 2(RS)-amino-4(RS)-phosphonopentanoic acid [79469-40-2]) were more potent as displacers of I binding than as inhibitors of synaptic transmission in the lateral perforant path; however, the L-isomer of I was equipotent in both assays. The ligand specificity in binding to the I site is discussed in relation to the regulation of the lateral perforant pathway and the pharmacol. of glutamate receptors.

IT 56-84-8, biological studies 56-86-0, biological studies 487-79-6

492-27-3 1783-96-6 6893-26-1 51276-47-2 52809-07-1 65914-80-9

78405-44-4 79055-68-8 79469-40-2 95742-06-6

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(aminophosphonobutanoate binding to brain response to)

ACCESSION NUMBER: 1985:197823 CAPLUS
 DOCUMENT NUMBER: 102:197823
 TITLE: Displacement of DL-[3H]-2-amino-4-phosphonobutanoic acid ([3H]APB) binding with methyl-substituted APB analogs and glutamate agonists
 AUTHOR(S): Robinson, Michael B.; Crooks, Stephen L.; Johnson, Rodney L.; Koerner, James F.
 CORPORATE SOURCE: Med. Sch., Univ. Minnesota, Minneapolis, MN, 55455, USA
 SOURCE: Biochemistry (1985), 24(10), 2401-5
 CODEN: BICHAW; ISSN: 0006-2960
 DOCUMENT TYPE: Journal
 LANGUAGE: English

ABSTRACT:

The binding of DL-2-amino-4-phosphonobutanoic acid (I) [20263-07-4] to rat brain synaptic membranes was saturable ($K_d = 6.0 \mu\text{M}$; $B_{\text{max}} = 380 \text{ pmol/mg/protein}$), Ca^{2+} - and Cl^- -dependent, and diminished upon freezing the membrane preparation. The L-isomer of I [23052-81-5], L-glutamic acid [56-86-0], and L-aspartic acid [56-84-8] were more potent as displacers of I binding than the resp. D-isomers. With the exception of kynurenic acid [492-27-3], all the other compds. examined (L- and D-glutamic acid [6893-26-1], L-glutamate tetrazole [65914-80-9], D-2-amino-5-phosphonopentanoic acid [79055-68-8], 2(RS)-amino-2-methyl-4-phosphonobutenoic acid [78405-44-4], DL-2-amino-4-(methylphosphino)butenoic acid [53369-07-6], 2(RS)-amino-3(RS)-methyl-4-phosphonobutanoic acid [95742-06-6], and 2(RS)-amino-4(RS)-phosphonopentanoic acid [79469-40-2]) were more potent as displacers of I binding than as inhibitors of synaptic transmission in the lateral perforant path; however, the L-isomer of I was equipotent in both assays. The ligand specificity in binding to the I site is discussed in relation to the regulation of the lateral perforant pathway and the pharmacol. of glutamate receptors.

L3 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

TI Synthesis and properties of phosphinothricin derivatives

IT 89916-00-7D, diester

RL: RCT (Reactant); RACT (Reactant or reagent)

... (reaction of, with tribenzylhexahydrotriazine)

ACCESSION NUMBER: 1984:174931 CAPLUS
 DOCUMENT NUMBER: 100:174931
 TITLE: Synthesis and properties of phosphinothricin derivatives
 AUTHOR(S): Maier, Ludwig; Rist, Guenter; Lea, Peter J.
 CORPORATE SOURCE: Agric. Div., Ciba-Geigy Ltd., Basel, Switz.
 SOURCE: Phosphorus and Sulfur and the Related Elements (1983), 18(1-2-3), 349-52
 CODEN: PREEDF; ISSN: 0308-664X
 DOCUMENT TYPE: Journal
 LANGUAGE: English

ABSTRACT:

Michaelis-Aruzov reaction of $\text{ClCH}_2\text{CH}_2\text{P}(\text{OEt})_2$ with RX [$\text{R} = \text{H}, \text{MeOCH}_2, \text{HO}_2\text{CCH}_2, \text{HO}_2\text{CCH}(\text{NH}_2)\text{CH}_2\text{CH}_2, \text{PhCH}_2, \text{p-BrC}_6\text{H}_4\text{CH}_2$], followed by treatment with (acylamino)malonates gave phosphinothricin derivs., $\text{RP}(\text{O})(\text{OH})\text{CH}_2\text{CH}(\text{NH}_2)\text{CO}_2\text{H}$ (I). I with different substituents on the N atom were obtained by base-catalyzed addition of substituted aminomalonates with Me vinylphosphinates, followed by hydrolysis. Also prepared was the isomer $\text{MeP}(\text{O})(\text{OH})\text{CH}_2\text{CH}(\text{CO}_2\text{H})\text{CH}_2\text{NH}_2$. I were purified by silylation with $(\text{Me}_3\text{Si})_2\text{NH}$, followed by distillation and hydrolysis.

L3 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

TI Organic phosphorus compounds. 76. Synthesis and properties of phosphinothricin derivatives

IT 89222-43-5

RL: RCT (Reactant); RACT (Reactant or reagent)
(reactions of)

ACCESSION NUMBER: 1984:121198 CAPLUS

DOCUMENT NUMBER: 100:121198

TITLE: Organic phosphorus compounds. 76. Synthesis and properties of phosphinothricin derivatives

AUTHOR(S): Maier, Ludwig; Lea, Peter J.

CORPORATE SOURCE: Agric. Div., Ciba-Geigy Ltd., Basel, Switz.

SOURCE: Phosphorus and Sulfur and the Related Elements (1983), 17(1), 1-19

CODEN: PREEDF; ISSN: 0308-664X

DOCUMENT TYPE: Journal

LANGUAGE: English

ABSTRACT:

Six phosphinothricin derivs. $\text{RP(O)(OH)CH}_2\text{CH}_2\text{CH(NH}_2\text{)CO}_2\text{H}$ (R = substituted benzyl, HO_2CCH_2 , MeOCH_2) were prepared by Michaelis-Arbuzov reaction of $\text{Cl(CH}_2)_2\text{P(OEt)}_2$ with RX (same R; X = halide) to give $\text{RP(O)(OEt)CH}_2\text{CH}_2\text{Cl}$, dehydrochlorination of the last with Et_3N to give vinylphosphinates RP(O)(OEt)CH:CH_2 , treatment of the last with $\text{AcNHCH(CO}_2\text{Et)}_2$, followed by hydrolysis in concentrated HCl. Also, seven $\text{MeP(O)(OH)CH}_2\text{CH}_2\text{CH(NRR}_1\text{)CO}_2\text{H}$ [R = Me, 3,4-ClMeC₆H₃, R₁ = CH₂Ph, H; RR₁ = (CH₂)_n (n = 4, 5, 6), (CH₂)₂CHMe(CH₂)₂, (CH₂)₂O(CH₂)₂] were prepared by base-catalyzed addition of $\text{MeP(O)(OMe)CH:CH}_2$ with $\text{RNR}_1\text{CH(CO}_2\text{Et)}_2$, followed by hydrolysis. The activity of some of the phosphinothricin analogs as glutamine synthetase inhibitors and contact herbicides is reported.

L3 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

TI Inhibition of rat liver glutamine synthetase by phosphonic analogs of glutamic acid

IT 56-85-9D, phosphonic analogs 56-86-0D, phosphonic analogs 6323-99-5

18865-31-1 51276-47-2 65482-86-2 73870-68-5 73870-69-6

78405-44-4 78405-48-8 78432-42-5 81746-56-7 115692-97-2

153605-27-7

RL: BIOL (Biological study)

(glutamine synthetase inhibition by)

ACCESSION NUMBER: 1981:457044 CAPLUS

DOCUMENT NUMBER: 95:57044

TITLE: Inhibition of rat liver glutamine synthetase by phosphonic analogs of glutamic acid

AUTHOR(S): Lejczak, B.; Starzemska, H.; Mastalerz, P.

CORPORATE SOURCE: Inst. Org. Phys. Chem., Tech. Univ., Wroclaw, PL-50370, Pol.

SOURCE: Experientia (1981), 37(5), 461-2

CODEN: EXPEAM; ISSN: 0014-4754

DOCUMENT TYPE: Journal

LANGUAGE: English

ABSTRACT:

Analogues of glutamic acid, α -methylglutamic acid, and glutamine in which the α - or γ -COOH groups are replaced by PO_3H_2 or P(O)(OH)_2 groups competitively inhibit rat liver glutamine synthetase. The K_i values are comparable to or lower than K_m for L-glutamate.

L3 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

TI Cytostatic activity in vitro of cycloleucine, aspartic acid and glutamic acid phosphonic analogs

IT 52-52-8 5652-28-8 5652-40-4 6323-99-5 18865-31-1 51276-47-2

52112-12-6 61341-13-7 61341-14-8 67398-11-2 67550-64-5

67550-65-6 67550-68-9 67550-69-0 73870-68-5 73870-71-0
75878-71-6 78405-44-4

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(cytostatic activity of)

ACCESSION NUMBER: 1981:140 CAPLUS

DOCUMENT NUMBER: 94:140

TITLE: Cytostatic activity in vitro of cycloleucine, aspartic acid and glutamic acid phosphonic analogs

AUTHOR(S): Dus, Danuta; Salwa, Jan; Mastalerz, Przemyslaw

CORPORATE SOURCE: Inst. Immunol. Exp. Therapy, Polish Acad. Sci.,
Wroclaw, Pol.

SOURCE: Archivum Immunologiae et Therapiae Experimentalis
(1980), 28(3), 433-8

CODEN: AITEAT; ISSN: 0004-069X

DOCUMENT TYPE: Journal

LANGUAGE: English

ABSTRACT:

Cytostatic activity of 18-new phosphonic acid derivative of cycloleucine, aspartic acid, and glutamic acid was tested against human KB and mouse L1210s leukemia cell lines in vitro. Four of the tested compds. revealed their cytostatic activity at 10 µg/mL.

=> FIL REGISTRY

COST IN U.S. DOLLARS

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TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

34.69

35.80

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

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REG - RN
 SAM - Index Name, MF, and structure - no RN
 FIDE - All substance data, except sequence data
 IDE - FIDE, but only 50 names
 SQIDE - IDE, plus sequence data
 SQIDE3 - Same as SQIDE, but 3-letter amino acid codes are used
 SQD - Protein sequence data, includes RN
 SQD3 - Same as SQD, but 3-letter amino acid codes are used
 SQN - Protein sequence name information, includes RN

 CALC - Table of calculated properties
 EPROP - Table of experimental properties
 PROP - EPROP and CALC

Any CA File format may be combined with any substance format to obtain CA references citing the substance. The substance formats must be cited first. The CA File predefined formats are:

ABS -- Abstract
 APPS -- Application and Priority Information
 BIB -- CA Accession Number, plus Bibliographic Data
 CAN -- CA Accession Number
 CBIB -- CA Accession Number, plus Bibliographic Data (compressed)
 IND -- Index Data
 IPC -- International Patent Classification
 PATS -- PI, SO
 STD -- BIB, IPC, and NCL

 IABS -- ABS, indented, with text labels
 IBIB -- BIB, indented, with text labels
 ISTD -- STD format, indented

 OBIB ----- AN, plus Bibliographic Data (original)
 OIBIB ----- OBIB, indented with text labels

 SBIB ----- BIB, no citations
 SIBIB ----- IBIB, no citations

The ALL format gives FIDE BIB ABS IND RE, plus sequence data when it is available.

The MAX format is the same as ALL.

The IALL format is the same as ALL with BIB ABS and IND indented, with text labels.

For additional information, please consult the following help messages:

HELP DFIELDS -- To see a complete list of individual display fields.
 HELP FORMATS -- To see detailed descriptions of the predefined formats.
 ENTER DISPLAY FORMAT (IDE):END

=> DIS L2 1- RN SAM
 'SAM' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'

The following are valid formats:

Substance information can be displayed by requesting individual fields or predefined formats. The predefined substance formats

are: (RN = CAS Registry Number)

REG - RN
 SAM - Index Name, MF, and structure - no RN
 FIDE - All substance data, except sequence data
 IDE - FIDE, but only 50 names
 SQIDE - IDE, plus sequence data
 SQIDE3 - Same as SQIDE, but 3-letter amino acid codes are used
 SQD - Protein sequence data, includes RN
 SQD3 - Same as SQD, but 3-letter amino acid codes are used
 SQN - Protein sequence name information, includes RN

 CALC - Table of calculated properties
 EPROP - Table of experimental properties
 PROP - EPROP and CALC

Any CA File format may be combined with any substance format to obtain CA references citing the substance. The substance formats must be cited first. The CA File predefined formats are:

ABS -- Abstract
 APPS -- Application and Priority Information
 BIB -- CA Accession Number, plus Bibliographic Data
 CAN -- CA Accession Number
 CBIB -- CA Accession Number, plus Bibliographic Data (compressed)
 IND -- Index Data
 IPC -- International Patent Classification
 PATS -- PI, SO
 STD -- BIB, IPC, and NCL

 IABS -- ABS, indented, with text labels
 IBIB -- BIB, indented, with text labels
 ISTD -- STD format, indented

 OBIB ----- AN, plus Bibliographic Data (original)
 OIBIB ----- OBIB, indented with text labels

 SBIB ----- BIB, no citations
 SIBIB ----- IBIB, no citations

The ALL format gives FIDE BIB ABS IND RE, plus sequence data when it is available.

The MAX format is the same as ALL.

The IALL format is the same as ALL with BIB ABS and IND indented, with text labels.

For additional information, please consult the following help messages:

HELP DFIELDS -- To see a complete list of individual display fields.
 HELP FORMATS -- To see detailed descriptions of the predefined formats.
 ENTER DISPLAY FORMAT (IDE):END

=> FIL CAPLUS

| | | |
|--|------------|---------|
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| FULL ESTIMATED COST | 0.88 | 36.68 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| CA SUBSCRIBER PRICE | 0.00 | -8.25 |

FILE 'CAPLUS' ENTERED AT 09:47:14 ON 18 JUL 2006

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
 COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 18 Jul 2006 VOL 145 ISS 4
 FILE LAST UPDATED: 17 Jul 2006 (20060717/ED)

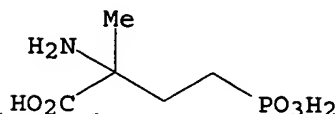
Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/infopolicy.html>

=> DIS L3 1 HITSEQ

THE ESTIMATED COST FOR THIS REQUEST IS 7.05 U.S. DOLLARS
 DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

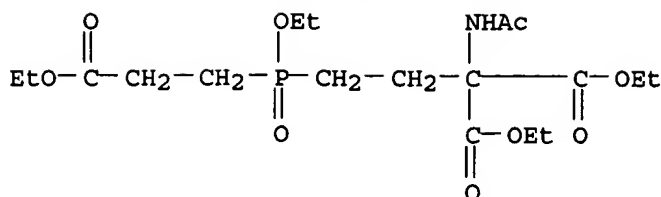
L3 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
 IT 78405-44-4, 2-Amino-2-methyl-4-phosphonobutanoic acid
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (enzymic synthesis of enantiomers of 2-amino-2-methyl-4-phosphonobutyric acid)
 RN 78405-44-4 CAPLUS
 CN Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)



=> DIS L3 2 HITSEQ

THE ESTIMATED COST FOR THIS REQUEST IS 7.05 U.S. DOLLARS
 DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L3 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
 IT 856766-89-7P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (asym. synthesis of pseudo-γ-glutamylglycine phosphinic acid pseudopeptides via penicillamidase catalyzed hydrolysis)
 RN 856766-89-7 CAPLUS
 CN Propanedioic acid, (acetyl amino)[2-[ethoxy(3-ethoxy-3-oxopropyl)phosphinyl]ethyl]-, diethyl ester (9CI) (CA INDEX NAME)



=> DIS L3 3 HITSEQ

THE ESTIMATED COST FOR THIS REQUEST IS 7.05 U.S. DOLLARS

DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

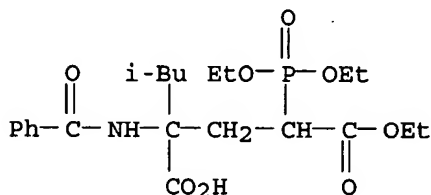
L3 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

IT 663943-17-7P

RL: SPN-(Synthetic preparation); PREP (Preparation)
(synthesis of α -alkyl- γ -phosphonoglutamic acids)

RN 663943-17-7 CAPLUS

CN Glutamic acid, N-benzoyl-4-(diethoxyphosphinyl)-2-(2-methylpropyl)-, 5-ethyl ester (9CI) (CA INDEX NAME)



=> DIS L3 4 HITSEQ

THE ESTIMATED COST FOR THIS REQUEST IS 7.05 U.S. DOLLARS

DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

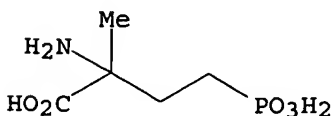
L3 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

IT 78405-44-4

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(metabotropic glutamate receptors ligand-binding site conservation during evolution)

RN 78405-44-4 CAPLUS

CN Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)



=> DIS L3 5 HITSEQ

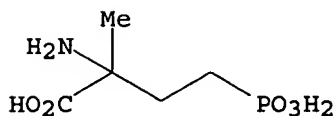
THE ESTIMATED COST FOR THIS REQUEST IS 7.05 U.S. DOLLARS

DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L3 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

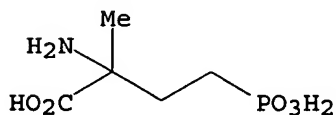
229

IT 78405-44-4
RL: BIOL (Biological study)
(quisqualic acid-sensitive AP4 receptor binding by, in CA1 hippocampus,
structure in relation to)
RN 78405-44-4 CAPLUS
CN Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)



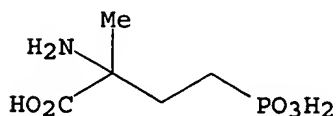
=> DIS L3 6 HITSEQ
THE ESTIMATED COST FOR THIS REQUEST IS 7.05 U.S. DOLLARS
DO-YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L3 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
IT 78405-44-4
RL: BIOL (Biological study)
(hippocampus synaptic neurotransmission inhibition by, mol. structure
in relation to)
RN 78405-44-4 CAPLUS
CN Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)



=> DIS L3 7 HITSEQ
THE ESTIMATED COST FOR THIS REQUEST IS 7.05 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L3 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
IT 78405-44-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); BIOL (Biological study)
(aminophosphonobutanoate binding to brain response to)
RN 78405-44-4 CAPLUS
CN Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

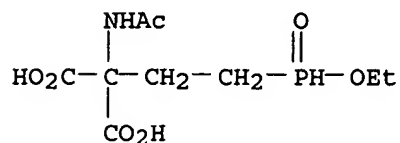


=> DIS L3 8 HITSEQ
THE ESTIMATED COST FOR THIS REQUEST IS 7.05 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L3 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

229

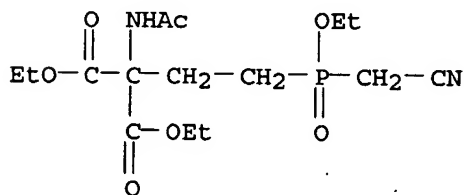
IT 89916-00-7D, diester
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction of, with tribenzylhexahydrotriazine)
 RN 89916-00-7 CAPLUS
 CN Propanedioic acid, (acetylamino) [2-(ethoxyphosphinyl)ethyl] - (9CI) (CA INDEX NAME)



=> DIS L3 9 HITSEQ

THE ESTIMATED COST FOR THIS REQUEST IS 7.05 U.S. DOLLARS
 DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

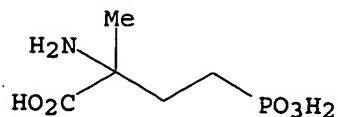
L3 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
 IT 89222-43-5
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reactions of)
 RN 89222-43-5 CAPLUS
 CN Propanedioic acid, (acetylamino) [2-[(cyanomethyl)ethoxyphosphinyl]ethyl] -, diethyl ester (9CI) (CA INDEX NAME)



=> DIS L3 10 HITSEQ

THE ESTIMATED COST FOR THIS REQUEST IS 7.05 U.S. DOLLARS
 DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L3 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
 IT 78405-44-4
 RL: BIOL (Biological study)
 (glutamine synthetase inhibition by)
 RN 78405-44-4 CAPLUS
 CN Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)



=> DIS L3 11 HITSEQ

THE ESTIMATED COST FOR THIS REQUEST IS 7.05 U.S. DOLLARS

229

DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

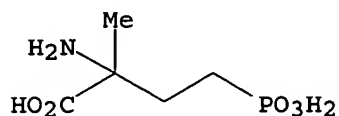
L3 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

IT 78405-44-4

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(cytostatic activity of)

RN 78405-44-4 CAPLUS

CN Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)



=> logoff

ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF

LOGOFF? (Y)/N/HOLD:Y

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

26.99

63.67

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

0.00

-8.25

STN INTERNATIONAL LOGOFF AT 09:48:28 ON 18 JUL 2006

Dialog level 05.12.03D

Last logoff: 12jul06 16:08:22

Logon file001 17jul06 15:25:21

*** ANNOUNCEMENTS ***

NEW FILES RELEASED

***Trademarkscan - South Korea (File 655)

***Regulatory Affairs Journals (File 183)

***Index Chemicus (File 302)

***Inspec (File 202)

RESUMED UPDATING

***File 141, Reader's Guide Abstracts

RELOADS COMPLETED

***File 516, D&B--Dun's Market Identifiers

***File 523, D&B European Dun's Market Identifiers

***File 531, American Business Directory

*** MEDLINE has been reloaded with the 2006 MeSH (Files 154 & 155)

*** The 2005 reload of the CLAIMS files (Files 340, 341, 942)

is now available online.

DATABASES REMOVED

***File 196, FINDEX

***File 468, Public Opinion Online (POLL)

Chemical Structure Searching now available in Prous Science Drug Data Report (F452), Prous Science Drugs of the Future (F453), IMS R&D Focus (F445/955), Pharmaprojects (F128/928), Beilstein Facts (F390), Derwent Chemistry Resource (F355) and Index Chemicus (File 302).

>>>For the latest news about Dialog products, services, content<<<

>>>and events, please visit What's New from Dialog at <<<

>>><http://www.dialog.com/whatsnew/>. You can find news about<<<

>>>a specific database by entering HELP NEWS <file number>.<<<

* * *

File 1:ERIC 1966-2006/June

(c) format only 2006 Dialog

| Set | Items | Description |
|-----|-------|-------------|
|-----|-------|-------------|

| | | |
|-----|-------|-------|
| --- | ----- | ----- |
|-----|-------|-------|

Cost is in DialUnits

?

Terminal set to DLINK

? b 5

17jul06 15:25:49 User291213 Session D64.1

\$0.39 0.112 DialUnits File1

\$0.39 Estimated cost File1

\$0.11 TELNET

\$0.50 Estimated cost this search

\$0.50 Estimated total session cost 0.112 DialUnits

File 5:Biosis Previews(R) 1969-2006/Jul W2

(c) 2006 The Thomson Corporation

| Set | Items | Description |
|-----|-------|-------------|
|-----|-------|-------------|

| | | |
|-----|-------|-------|
| --- | ----- | ----- |
|-----|-------|-------|


```

? s cyclodextrin?(S) (tocopherol or (vitamin(W)E)
>>>Unmatched parentheses
? s cyclodextrin?(S) (tocopherol or (vitamin(W)E))
      9950 CYCLODEXTRIN?
      16552 TOCOPHEROL
      122584 VITAMIN
      766074 E
      24086 VITAMIN(W)E
S1      20 CYCLODEXTRIN?(S) (TOCOPHEROL OR (VITAMIN(W)E))
? rd
      S2      20 RD (unique items)
? t s2/free/all

```

2/6/1
0015320770 BIOSIS NO.: 200510015270
Solubilization of tocopherols by using cyclization reaction with
cyclodextrin glucanotransferase
2005

2/6/2
0015211361 BIOSIS NO.: 200500117539
Xanthophylls and alpha-tocopherol decrease UVB-induced lipid peroxidation
and stress signaling in human lens epithelial cells
2004

2/6/3
0014949525 BIOSIS NO.: 200400320282
Uptake and transport of high-density lipoprotein (HDL) and HDL-associated
alpha-tocopherol by an in vitro blood-brain barrier model
2004

2/6/4
0014914408 BIOSIS NO.: 200400285165
Lutein and zeaxanthin decrease UVB-induced stress signaling in human lens
epithelial cells
2004

2/6/5
0014807806 BIOSIS NO.: 200400178563
Solubilizing excipients in oral and injectable formulations.
2004

2/6/6
0014614795 BIOSIS NO.: 200300583514
Antioxidant activities of natural vitamin E formulations.
2003

2/6/7
0014424517 BIOSIS NO.: 200300381794
Use of cyclodextrin as a vehicle for loading human lens epithelial and
human ciliary body cells with xanthophylls and alpha- tocopherol.
2003

2/6/8

0014358463 BIOSIS NO.: 200300317182

Action of pyrethrum-based formulations against grain weevils.
2003

2/6/9

0013655657 BIOSIS NO.: 200200249168

Development and validation of oxygen radical absorbance capacity assay for
lipophilic antioxidants using randomly methylated beta-cyclodextrin as
the solubility enhancer
2002

2/6/10

0013568114 BIOSIS NO.: 200200161625

Modulation of human lymphocyte proliferative response with aging
2002

2/6/11

0012678971 BIOSIS NO.: 200000397284

Oxidation of d-alpha-tocopherol in aqueous solution. Formation of colored
products
1999

2/6/12

0012530379 BIOSIS NO.: 200000248692

Kinetic behavior of three preparations of alpha-tocopherol after oral
administration to postpubertal heifers
2000

2/6/13

0012330032 BIOSIS NO.: 200000048345

Cis/trans isomers of tocotrienols: Occurrence and bioavailability
1999

2/6/14

0011634276 BIOSIS NO.: 199800428523

Oxidative damage induced by the fullerene C60 on photosensitization in rat
liver microsomes
1998

2/6/15

0011466418 BIOSIS NO.: 199800260665

Neurotoxicity of cholesterol oxides on cultured cerebellar granule cells
1998

2/6/16

0011441586 BIOSIS NO.: 199800235833

Neurotoxicity of 25-OH-cholesterol on sympathetic neurons
1998

2/6/17

0011344881 BIOSIS NO.: 199800139128
Neurotoxicity of 25-OH-cholesterol on NGF-differentiated PC12 cells
1998

2/6/18
0011175699 BIOSIS NO.: 199799809759
Comparison of the separation of fat-soluble vitamins using
beta-cyclodextrins in high-performance liquid chromatography and micellar
electrokinetic chromatography
1997

2/6/19
0009156985 BIOSIS NO.: 199497178270
Bitterness-suppressive formulation of benexate hydrochloride betadex
prepared by hot melt granulation
1993

2/6/20
0006780276 BIOSIS NO.: 198988095391
SUPPRESSION OF FISHY ODOR IN SARDINE MEAT
1989

? s s2 and skin
20 S2
250312 SKIN
S3 0 S2 AND SKIN
? s s2 and (derma\$ or sunscreen)
20 S2
0 DERMA\$
1754 SUNSCREEN
S4 0 S2 AND (DERMA\$ OR SUNSCREEN)
? sf all
>>>SELECT FILES not supported.
? b 411
17jul06 15:29:56 User291213 Session D64.2
\$5.80 0.982 DialUnits File5
\$0.00 20 Type(s) in Format 6
\$0.00 20 Types
\$5.80 Estimated cost File5
\$1.33 TELNET
\$7.13 Estimated cost this search
\$7.63 Estimated total session cost 1.095 DialUnits

File 411:DIALINDEX(R)

DIALINDEX(R)
(c) 2006 Dialog

*** DIALINDEX search results display in an abbreviated ***
*** format unless you enter the SET DETAIL ON command. ***
? sf all
You have 562 files in your file list.
(To see banners, use SHOW FILES command)
? s cyclodextrin?(S)(tocopherol or (vitamin(W)E))

Your SELECT statement is:
s cyclodextrin?(S)(tocopherol or (vitamin(W)E))

| Items | File |
|--------------|--|
| 20 | 5: Biosis Previews(R)_1969-2006/Jul W2 |
| 1 | 7: Social SciSearch(R)_1972-2006/Jul W2 |
| 1 | 8: Ei Compendex(R)_1970-2006/Jul W2 |
| 4 | 9: Business & Industry(R)_Jul/1994-2006/Jul 14 |
| 2 | 10: AGRICOLA_70-2006/May |
| 1 | 13: BAMP_2006/Jul W2 |
| 3 | 15: ABI/Inform(R)_1971-2006/Jul 17 |
| 6 | 16: Gale Group PROMT(R)_1990-2006/Jul 14 |
| 3 | 20: Dialog Global Reporter_1997-2006/Jul 17 |
| 4 | 24: CSA Life Sciences Abstracts_1966-2006/May |
| 29 | 34: SciSearch(R) Cited Ref Sci_1990-2006/Jul W2 |
| 1 | 35: Dissertation Abs Online_1861-2006/Jun |
| 7 | 50: CAB Abstracts_1972-2006/Jun |
| 8 | 51: Food Sci.&Tech.Abs_1969-2006/Jul W2 |
| 10 | 53: FOODLINE(R): Science_1972-2006/Jul 12 |
| Examined 50 | files |
| 1 | 67: World Textiles_1968-2006/Jul |
| 10 | 71: ELSEVIER BIOBASE_1994-2006/Jul W3 |
| 18 | 73: EMBASE_1974-2006/Jul 17 |
| 4 | 74: Int.Pharm.Abs_1970-2006/May B2 |
| 1 | 79: Foods Adlibra(TM)_1974-2002/Apr |
| 1 | 88: Gale Group Business A.R.T.S._1976-2006/Jul 05 |
| 12 | 94: JICST-EPlus_1985-2006/Apr W3 |
| 4 | 95: TEME-Technology & Management_1989-2006/Jul W3 |
| 2 | 112: UBM Industry News_1998-2004/Jan 27 |
| Examined 100 | files |
| 1 | 135: NewsRx Weekly Reports_1995-2006/Jul W2 |
| 12 | 144: Pascal_1973-2006/Jun W4 |
| 3 | 148: Gale Group Trade & Industry DB_1976-2006/Jul 14 |
| 16 | 155: MEDLINE(R)_1950-2006/Jul 17 |
| 8 | 156: ToxFile_1965-2006/Jul W2 |
| 3 | 159: Cancerlit_1975-2002/Oct |
| 3 | 162: Global Health_1983-2006/Jun |
| 1 | 172: EMBASE Alert_2006/Jul 17 |
| 2 | 180: Federal Register_1985-2006/Jul 14 |
| 1 | 203: AGRIS_1974-2006/Mar |
| Examined 150 | files |
| 3 | 240: PAPERCHEM_1967-2006/Jul W3 |
| 1 | 248: PIRA_1975-2006/Jun W4 |
| 1 | 266: FEDRIP_2005/Dec |
| 2 | 280: ONTAP Derwent World Patents Index |
| Examined 200 | files |
| 1 | 285: BioBusiness(R)_1985-1998/Aug W1 |
| 1 | 302: INDEX CHEMICUS_1993-200628 |
| 2 | 305: Analytical Abstracts_1980-2006/Jul W1 |
| 1 | 315: ChemEng & Biotec Abs_1970-2006/Jun |
| 1 | 319: Chem Bus NewsBase_1984-2006/Jul 17 |
| 70 | 324: German Patents Fulltext_1967-200627 |
| 1 | 331: Derwent WPI First View UD=200645 |
| 32 | 340: CLAIMS(R)/US Patent_1950-06/Jul 13 |
| 10 | 342: Derwent Patents Citation Indx_1978-05/200641 |
| 2 | 344: Chinese Patents Abs_Jan 1985-2006/Jan |
| 5 | 345: Inpadoc/Fam.& Legal Stat_1968-2006/UD=200628 |
| 38 | 347: JAPIO_Dec 1976-2005/Dec(Updated 060404) |
| 108 | 348: EUROPEAN PATENTS_1978-2006/ 200628 |
| 489 | 349: PCT FULLTEXT_1979-2006/UB=20060713,UT=20060706 |
| 1 | 355: Derwent Chemistry Resource_UD=200642 |
| 3 | 357: Derwent Biotech Res._1982-2006/Jul W2 |
| 1 | 358: Current BioTech Abs_1983-2006/Jan |

Examined 250 files

20 377: Derwent Drug File_1983-2006/Jun W3
2 390: Beilstein Abstracts_2006/Q2
2 391: Beilstein Reactions_2006/Q2
4 393: Beilstein Abstracts_2006/Q2
7 398: Chemsearch_1957-2006/Jun
37 399: CA SEARCH(R)_1967-2006/UD=14504
30 440: Current Contents Search(R)_1990-2006/Jul 17
1 446: IMS-New Product Focus_1982-2006/May

Examined 300 files

1 484: Periodical Abs Plustext_1986-2006/Jul W2

Examined 350 files

3 570: Gale Group MARS(R)_1984-2006/Jul 14

Examined 400 files

2 613: PR Newswire_1999-2006/Jul 17
1 619: Asia Intelligence Wire_1995-2006/Jul 16
3 636: Gale Group Newsletter DB(TM)_1987-2006/Jul 14

Processing

1268 654: US Pat.Full._1976-2006/Jul 13

Examined 450 files

Examined 500 files

3 763: Freedonia Market Res._1990-2006/Jul
2 764: BCC Market Research_1989-2006/Jul
2 766: (R)Kalorama Info Market Res._1993-2000/Aug

Examined 550 files

1 990: NewsRoom Current_Mar 1 -2006/Jul 17
4 992: NewsRoom 2005
2 993: NewsRoom 2004
3 996: NewsRoom 2000-2001

76 files have one or more items; file list includes 562 files.

? b 34 348 349 324 654

17jul06 15:35:40 User291213 Session D64.3

\$36.24 13.674 DialUnits File411

\$36.24 Estimated cost File411

\$1.60 TELNET

\$37.84 Estimated cost this search

\$45.47 Estimated total session cost 14.769 DialUnits

SYSTEM:OS - DIALOG OneSearch

File 34:SciSearch(R) Cited Ref Sci 1990-2006/Jul W2

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File 348:EUROPEAN PATENTS 1978-2006/ 200628

(c) 2006 European Patent Office

***File 348: For important information about IPCR/8 and forthcoming changes to the IC= index, see HELP NEWSIPCR.**

File 349:PCT FULLTEXT 1979-2006/UB=20060713,UT=20060706

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***File 349: For important information about IPCR/8 and forthcoming changes to the IC= index, see HELP NEWSIPCR.**

File 324:German Patents Fulltext 1967-200627

(c) 2006 Univentio

***File 324: For important information about IPCR/8 and forthcoming changes to the IC= index, see HELP NEWSIPCR.**

File 654:US Pat.Full. 1976-2006/Jul 13

(c) Format only 2006 Dialog

***File 654: IPCR/8 classification codes now searchable in 2006 records.**
For information about IC= index changes, see HELP NEWSIPCR.

| Set | Items | Description |
|---|---------|---|
| --- | ----- | ----- |
| ? s cyclodextrin?(S)(tocopherol or (vitamin(W)E)) | | |
| Processing | | |
| Processing | | |
| | 60796 | CYCLODEXTRIN? |
| | 50305 | TOCOPHEROL |
| | 180876 | VITAMIN |
| | 6614735 | E |
| | 59100 | VITAMIN(W)E |
| S1 | 1964 | CYCLODEXTRIN?(S)(TOCOPHEROL OR (VITAMIN(W)E)) |
| ? s s1 and (skin or derm\$ or sunscreen) | | |
| | 1964 | S1 |
| | 661253 | SKIN |
| | 0 | DERM\$ |
| | 12620 | SUNSCREEN |
| S2 | 1447 | S1 AND (SKIN OR DERM\$ OR SUNSCREEN) |
| ? s (cyclodextrin?(S)(tocopherol or (vitamin(W)E)) NEAR(5) complex) | | |
| >>>Invalid syntax | | |
| ? s (cyclodextrin?(S)(tocopherol or (vitamin(W)E))NEAR(5)complex) | | |
| >>>Invalid syntax | | |
| ? s (cyclodextrin?(S)(tocopherol or (vitamin(W)E))(W)complex) | | |
| Processing | | |
| Processing | | |
| | 60796 | CYCLODEXTRIN? |
| | 50305 | TOCOPHEROL |
| | 180876 | VITAMIN |
| | 6614735 | E |
| | 59100 | VITAMIN(W)E |
| | 2212806 | COMPLEX |
| S3 | 3 | (CYCLODEXTRIN?(S)(TOCOPHEROL OR (VITAMIN(W)E))(W)COMPLEX) |
| ? t s3/free/all | | |
| >>>"FREE" is not a valid format name in file(s): 324, 348-349, 654 | | |
| ? t s3/3,k/all | | |

3/3,K/1 (Item 1 from file: 324)
 DIALOG(R)File 324:German Patents Fulltext
 (c) 2006 Univentio. All rts. reserv.

0003943877 **Image available**
2:1-Komplex aus beta- oder gamma-Cyclodextrin und alpha-Tocopherol
 Patent Applicant/Assignee: WACKER CHEMIE GMBH, DE
 Inventor(s): KUPKA MICHAELA, DE
 Patent and Priority Information (Country, Number, Date):
 Patent: DE 10200657 A1 20030724
 Application: DE 10200657 20020110
 Priority Application: DE 10200657 20020110 (DE 10200657)
 Publication Language: German
 Fulltext Word Count (English): 4520
 Fulltext Word Count (German) : 4181
 Fulltext Word Count (Both) : 8701

Fulltext Availability:
 Description (English machine translation)

Description (English machine translation)
 ... 1 complex is to be recognized clearly.
 Color of the complexes after 8 months

Ss- Cyclodextrin /- Tocopherol complex ; 1: 1; light yellow colouring;
Ss- Cyclodextrin /- Tocopherol complex ; 2: 1; almost knows; physical
mixture sss- Cyclodextrin /-Tocopherol 2: 1 intensive yellow colouring;
physical mixtures ss- Cyclodextrin /-Tocopherol 1: 1 intensive yellow
colouring.

Example 5

Determination of the stability in storage of...

...with 50oC

Manufacture a cream with 0,2% -Tocopherol content in a 1:1
-Cyclodextrin/- Tocopherol complex

0.4167 g of a -Cyclodextrin/-Tocopherol of complex 1: 1 (24%
-Tocopherol) with 24...

...HPLC was examined.

Manufacture a cream with 0,2% -Tocopherol content in 2: 1 -Cyclodextrin/-
Tocopherol complex

0.769 g of a -Cyclodextrin/-Tocopherol of complex 2: 1 (13% Tocopherol)
with 24...

3/3,K/2 (Item 1 from file: 654)
DIALOG(R)File 654:US Pat.Full.
(c) Format only 2006 Dialog. All rts. reserv.

0005653927 **IMAGE Available
Derwent Accession: 2004-432837
Cosmetic composition comprising a complex of cyclodextrin and vitamin F
Inventor: Regiert, Marlies, INV
Kupka, Michaela, INV
Assignee: Wacker-Chemie GmbH(03), Munich, DE
Correspondence Address: WILLIAM COLLARD COLLARD & ROE, P.C., 1077 NORTHERN
BOULEVARD, ROSLYN, NY, 11576, US

| | Publication Number | Kind | Date | Application Number | Filing Date |
|-------------|-----------------------|------|----------|-----------------------|----------------|
| Main Patent | US 20040096413 | A1 | 20040520 | US 2003712703 | 20031112 |
| Priority | | | | DE 10253042 | 20021114 |

Fulltext Word Count: 7083

Non-exemplary or Dependent Claim(s):

...chloride; 59.0% by weight of water; 1.5% by weight of [small gamma,
Greek]- cyclodextrin -[small alpha, Greek]- tocopherol complex ;
and 4.0% by weight of [small alpha, Greek]- cyclodextrin -linoleic
acid complex; and wherein each percent by weight is based upon
the total...

...weight of water; 1.70% by weight of [small gamma,
Greek]-cyclodextrin-[small alpha, Greek]- tocopherol complex ;
2.40% by weight of [small alpha, Greek]- cyclodextrin -linoleic acid
complex; 0.05% by weight of methylchloroisothiazolinone; and 0.30% by
weight of...

3/3,K/3 (Item 2 from file: 654)
DIALOG(R) File 654:US Pat.Full.
(c) Format only 2006 Dialog. All rts. reserv.

0005289174 **IMAGE Available
Derwent Accession: 2004-106475
2:1 Complex of beta- or gamma-cyclodextrin and alpha-tocopherol
Inventor: Marlies Regiert, INV
Michaela Kupka, INV
Assignee: WACKER-CHEMIE GmbH(03)
Correspondence Address: COLLARD & ROE, P.C., 1077 Northern Boulevard,
Roslyn, NY, 11576, US

| | Publication Number | Kind | Date | Application Number | Filing Date |
|-------------|-----------------------|------|----------|-----------------------|----------------|
| Main Patent | US 20030130231 | A1 | 20030710 | US 2002323019 | 20021219 |
| Priority | | | | DE 10200657 | 20020110 |

Fulltext Word Count: 6349

Description of the Invention:

...0093] [small beta, Greek]- **Cyclodextrin** /[small alpha, Greek]-
tocopherol complex 1:1 slight yellowing...

...0094] [small beta, Greek]-cyclodextrin/[small alpha, Greek]- **tocopherol**
complex 2:1 virtually white physical mixtures of [small beta, Greek]-
cyclodextrin /[small alpha, Greek]-tocopherol 2:1 intensive yellowing...

...Storage Stability of the [small gamma, Greek]-Cyclodextrin/[small alpha,
Greek]- **Tocopherol Complex** in a Cream at RT and at 50 degree C...

...alpha, Greek]-Tocopherol Content in a 1:1 [small gamma,
Greek]-Cyclodextrin/[small alpha, Greek]- **Tocopherol Complex**

[...]

...0121] 0.4167 g of a [small gamma, Greek]-cyclodextrin/[small alpha,
Greek]- **tocopherol complex** 1:1 (24% [small alpha, Greek]-tocopherol)
were dispersed with 24.7251 g of water...

...alpha, Greek]-Tocopherol Content in a 2:1 [small gamma,
Greek]-Cyclodextrin/[small alpha, Greek]- **Tocopherol Complex** :

[...]

...0123] 0.769 g of a [small gamma, Greek]-cyclodextrin/[small alpha,
Greek]- **tocopherol complex** 2:1 (13% [small alpha, Greek]-tocopherol)
were dispersed with 24.579 g of water

? cost

17jul06 15:42:02 User291213 Session D64.4
\$6.03 0.257 DialUnits File34
\$6.03 Estimated cost File34
\$4.49 0.829 DialUnits File348
\$4.49 Estimated cost File348
\$6.17 1.300 DialUnits File349
\$6.17 Estimated cost File349
\$3.74 0.748 DialUnits File324

\$1.70 1 Type(s) in Format 3
 \$1.70 1 Types
 \$5.44 Estimated cost File324
 \$19.91 3.374 DialUnits File654
 \$1.40 2 Type(s) in Format 3
 \$1.40 2 Types
 \$21.31 Estimated cost File654
 OneSearch, 5 files, 6.508 DialUnits FileOS
 \$1.86 TELNET
 \$45.30 Estimated cost this search
 \$90.77 Estimated total session cost 21.277 DialUnits

? logoff

17jul06 15:42:34 User291213 Session D64.4
 \$6.03 0.257 DialUnits File34
 \$6.03 Estimated cost File34
 \$4.49 0.829 DialUnits File348
 \$4.49 Estimated cost File348
 \$6.17 1.300 DialUnits File349
 \$6.17 Estimated cost File349
 \$3.74 0.748 DialUnits File324
 \$1.70 1 Type(s) in Format 3
 \$1.70 1 Types
 \$5.44 Estimated cost File324
 \$19.91 3.374 DialUnits File654
 \$1.40 2 Type(s) in Format 3
 \$1.40 2 Types
 \$21.31 Estimated cost File654
 OneSearch, 5 files, 6.508 DialUnits FileOS
 \$1.86 TELNET
 \$45.30 Estimated cost this search
 \$90.77 Estimated total session cost 21.277 DialUnits

Logoff: level 05.12.03 D 15:42:34

You are now logged off

37 654: US Pat.Full._1976-2006/Jul 13
Examined 450 files
Examined 500 files
1 745: Investext(R) PDF Index_1999--2006/Jul W3
Examined 550 files

93 files have one or more items; file list includes 562 files.
One or more terms were invalid in 226 files.

? b 5 73 35 34 144 155 24 440 357 162
18jul06 14:24:21 User291213 Session D65.2
\$11.07 4.179 DialUnits File411
\$11.07 Estimated cost File411
\$2.40 TELNET
\$13.47 Estimated cost this search
\$14.44 Estimated total session cost 4.416 DialUnits

SYSTEM:OS - DIALOG OneSearch
File 5:Biosis Previews(R) 1969-2006/Jul W2
(c) 2006 The Thomson Corporation
File 73:EMBASE 1974-2006/Jul 18
(c) 2006 Elsevier Science B.V.
File 35:Dissertation Abs Online 1861-2006/Jun
(c) 2006 ProQuest Info&Learning
File 34:SciSearch(R) Cited Ref Sci 1990-2006/Jul W2
(c) 2006 The Thomson Corp
File 144:Pascal 1973-2006/Jun W4
(c) 2006 INIST/CNRS
File 155:MEDLINE(R) 1950-2006/Jul 17
(c) format only 2006 Dialog
File 24:CSA Life Sciences Abstracts 1966-2006/May
(c) 2006 CSA.
File 440:Current Contents Search(R) 1990-2006/Jul 18
(c) 2006 The Thomson Corp
File 357:Derwent Biotech Res. _1982-2006/Jul W2
(c) 2006 The Thomson Corp.
File 162:Global Health 1983-2006/Jun
(c) 2006 CAB International

| Set | Items | Description |
|---|--------|---|
| --- | ----- | ----- |
| ? s au=((horwitz, M?) or (Horwitz M?)) | | |
| | 243 | AU=HORWITZ, M? |
| | 2286 | AU=HORWITZ M? |
| S1 | 2529 | AU=((HORWITZ, M?) OR (HORWITZ M?)) |
| ? s s1 and mycobacterium | | |
| | 2529 | S1 |
| | 280867 | MYCOBACTERIUM |
| S2 | 443 | S1 AND MYCOBACTERIUM |
| ? s s2 and (methionine or sulfoximine or phosphinothricin or glutamine) | | |
| | 443 | S2 |
| | 219111 | METHIONINE |
| | 19889 | SULFOXIMINE |
| | 3621 | PHOSPHINOTHRICIN |
| | 154190 | GLUTAMINE |
| S3 | 82 | S2 AND (METHIONINE OR SULFOXIMINE OR PHOSPHINOTHRICIN OR GLUTAMINE) |
| ? s s3 and anti(3n)bacter? | | |
| Processing | | |
| Processing | | |

Processing
Processed 10 of 10 files ...
Completed processing all files
82 S3
2439789 ANTI
5374442 BACTER?
174052 ANTI(3N)BACTER?
S4 2 S3 AND ANTI(3N)BACTER?
? t s4/free/all

4/8/1 (Item 1 from file: 155)
DIALOG(R)File 155:(c) format only 2006 Dialog. All rts. reserv.

14116641 PMID: 12496196

Inhibition of Mycobacterium tuberculosis glutamine synthetase as a novel antibiotic strategy against tuberculosis: demonstration of efficacy in vivo.

Jan 2003

Descriptors: *Anti - Bacterial Agents--therapeutic use--TU;
*Antitubercular Agents--therapeutic use--TU; *Glutamate-Ammonia Ligase
--antagonists and inhibitors--AI; *Methionine Sulfoximine --therapeutic
use--TU; *Mycobacterium tuberculosis--drug effects--DE; *Tuberculosis,
Pulmonary--drug therapy--DT; Animals; Anti - Bacterial Agents
--pharmacology--PD; Antitubercular Agents--pharmacology--PD; Colony Count,
Microbial; Disease Models, Animal; Drug Synergism; Guinea Pigs; Humans;
Isoniazid--therapeutic use--TU; Lung--microbiology--MI; . Methionine
Sulfoximine --pharmacology--PD; Microbial Sensitivity Tests;
Mycobacterium tuberculosis--enzymology--EN; Research Support, U.S. Gov't,
P.H.S.; Spleen--microbiology--MI; Tuberculosis, Pulmonary--microbiology--MI
CAS Registry No.: 0 (Anti-Bacterial Agents); 0 (Antitubercular Agents)
; 1982-67-8 (Methionine Sulfoximine); 54-85-3 (Isoniazid)
Enzyme No.: EC 6.3.1.2 (Glutamate-Ammonia Ligase)

4/8/2 (Item 2 from file: 155)
DIALOG(R)File 155:(c) format only 2006 Dialog. All rts. reserv.

12380229 PMID: 10224282

An inhibitor of exported Mycobacterium tuberculosis glutamine synthetase selectively blocks the growth of pathogenic mycobacteria in axenic culture and in human monocytes: extracellular proteins as potential novel drug targets.

May 3 1999

Descriptors: *Glutamate-Ammonia Ligase--antagonists and inhibitors--AI;
*Monocytes--microbiology--MI; *Mycobacterium tuberculosis --growth and
development--GD; Aminobutyric Acids--pharmacology--PD; Animals; Anti -
Bacterial Agents--pharmacology--PD; Cell Wall--metabolism--ME; Drug
Synergism; Enzyme Inhibitors--pharmacology--PD; Extracellular Space;
Glutamic Acid--metabolism--ME; Humans; Methionine Sulfoximine
--pharmacology--PD; Monocytes--drug effects--DE; Mycobacterium
tuberculosis--drug effects--DE; Peptidoglycan--metabolism--ME; Polyglutami
c Acid--metabolism--ME; Research Support, U.S. Gov't, P.H.S.; Sheep
CAS Registry No.: 0 (Aminobutyric Acids); 0 (Anti-Bacterial Agents);
0 (Enzyme Inhibitors); 0 (Peptidoglycan); 1982-67-8 (Methionine
Sulfoximine); 25513-46-6 (Polyglutamic Acid); 51276-47-2
(phosphinothricin); 56-86-0 (Glutamic Acid)
Enzyme No.: EC 6.3.1.2 (Glutamate-Ammonia Ligase)
? t s4/3,k/all

4/3,K/1 (Item 1 from file: 155)

DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

14116641 PMID: 12496196

Inhibition of Mycobacterium tuberculosis glutamine synthetase as a novel antibiotic strategy against tuberculosis: demonstration of efficacy in vivo.

Harth Gunter; Horwitz Marcus A

Department of Medicine, School of Medicine, University of California, Los Angeles, California 90095-1688, USA.

Infection and immunity (United States) Jan 2003, 71 (1) p456-64,
ISSN 0019-9567--Print Journal Code: 0246127

Contract/Grant No.: AI42925; AI; NIAID

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Inhibition of Mycobacterium tuberculosis glutamine synthetase as a novel antibiotic strategy against tuberculosis: demonstration of efficacy in vivo.

Harth Gunter; Horwitz Marcus A

... humankind's greatest killers, and new therapeutic strategies are needed to combat the causative agent, **Mycobacterium tuberculosis**, which is rapidly developing resistance to conventional antibiotics. Using the highly demanding guinea pig model of pulmonary tuberculosis, we have investigated the feasibility of inhibiting *M. tuberculosis* glutamine synthetase (GS), an enzyme that plays a key role in both nitrogen metabolism and cell...

... by aerosol with the highly virulent Erdman strain of *M. tuberculosis*, the GS inhibitor L- **methionine** -SR- **sulfoximine** (MSO) protected the animals against weight loss, a hallmark of tuberculosis, and against the growth...

Descriptors: *Anti - Bacterial Agents--therapeutic use--TU; *Antitubercular Agents--therapeutic use--TU; *Glutamate-Ammonia Ligase --antagonists and inhibitors--AI; * **Methionine Sulfoximine** --therapeutic use--TU; * **Mycobacterium tuberculosis**--drug effects--DE; *Tuberculosis, Pulmonary--drug therapy--DT; Animals; Anti - Bacterial Agents --pharmacology--PD; Antitubercular Agents--pharmacology--PD; Colony Count, Microbial; Disease Models, Animal; Drug Synergism; Guinea Pigs; Humans; Isoniazid--therapeutic use--TU; Lung--microbiology--MI; **Methionine Sulfoximine** --pharmacology--PD; Microbial Sensitivity Tests; **Mycobacterium tuberculosis**--enzymology--EN; Research Support, U.S. Gov't, P.H.S.; Spleen--microbiology--MI...

Chemical Name: Anti - Bacterial Agents; Antitubercular Agents; **Methionine Sulfoximine** ; Isoniazid; Glutamate-Ammonia Ligase

4/3,K/2 (Item 2 from file: 155)

DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

12380229 PMID: 10224282

An inhibitor of exported Mycobacterium tuberculosis glutamine synthetase selectively blocks the growth of pathogenic mycobacteria in axenic culture and in human monocytes: extracellular proteins as potential novel drug targets.

Harth G; Horwitz M A

Department of Medicine, University of California at Los Angeles School of Medicine, Los Angeles, California 90095, USA.

Journal of experimental medicine (UNITED STATES) May 3 1999, 189 (9) p1425-36, ISSN 0022-1007--Print Journal Code: 2985109R

Contract/Grant No.: AI 31338; AI; NIAID; AI 42925; AI; NIAID

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

An inhibitor of exported Mycobacterium tuberculosis glutamine synthetase selectively blocks the growth of pathogenic mycobacteria in axenic culture and in human monocytes...

Harth G; Horwitz M A

Mycobacterium tuberculosis and other pathogenic mycobacteria export abundant quantities of proteins into their extracellular milieu when growing either axenically or within phagosomes of host cells. One major extracellular protein, the enzyme **glutamine synthetase**, is of particular interest because of its link to pathogenicity. Pathogenic mycobacteria, but not...

...Interestingly, export of the enzyme is associated with the presence of a poly-L-glutamate/ **glutamine** structure in the mycobacterial cell wall. In this study, we investigated the influence of **glutamine synthetase** inhibitors on the growth of pathogenic and nonpathogenic mycobacteria and on the poly-L-glutamate/ **glutamine** cell wall structure. The inhibitor L- **methionine -S- sulfoximine** rapidly inactivated purified M. tuberculosis **glutamine synthetase**, which was 100-fold more sensitive to this inhibitor than a representative mammalian **glutamine synthetase**. Added to cultures of pathogenic mycobacteria, L- **methionine - S- sulfoximine** rapidly inhibited extracellular **glutamine synthetase** in a concentration-dependent manner but had only a minimal effect on cellular **glutamine synthetase**, a finding consistent with failure of the drug to cross the mycobacterial cell wall. Remarkably, the inhibitor selectively blocked the growth of pathogenic mycobacteria, all of which release **glutamine synthetase** extracellularly, but had no effect on nonpathogenic mycobacteria or nonmycobacterial microorganisms, none of which release **glutamine synthetase** extracellularly. The inhibitor was also bacteriostatic for M. tuberculosis in human mononuclear phagocytes (THP...

...perhaps underlying its bacteriostatic effect, the inhibitor markedly reduced the amount of poly-L-glutamate/ **glutamine** cell wall structure in M. tuberculosis. Although it is possible that **glutamine synthetase** inhibitors interact with additional extracellular proteins or structures, our findings support the concept that...

Descriptors: *Glutamate-Ammonia Ligase--antagonists and inhibitors--AI; *Monocytes--microbiology--MI; * **Mycobacterium tuberculosis** --growth and development--GD; Aminobutyric Acids--pharmacology--PD; Animals; **Anti - Bacterial Agents**--pharmacology--PD; Cell Wall--metabolism--ME; Drug Synergism; Enzyme Inhibitors--pharmacology--PD; Extracellular Space; Glutamic Acid--metabolism--ME; Humans; **Methionine Sulfoximine** --pharmacology--PD; Monocytes--drug effects--DE; **Mycobacterium tuberculosis**--drug effects--DE; Peptidoglycan--metabolism--ME; Polyglutamic Acid--metabolism--ME; Research Support, U.S...

Chemical Name: Aminobutyric Acids; **Anti - Bacterial Agents**; Enzyme Inhibitors; Peptidoglycan; **Methionine Sulfoximine** ; Polyglutamic Acid; **phosphinothricin** ; Glutamic Acid; Glutamate-Ammonia Ligase

? ds

```

Set      Items  Description
S1       2529   AU=((HORWITZ, 'M?') OR (HORWITZ M?))
S2       443    S1 AND MYCOBACTERIUM
S3       82     S2 AND (METHIONINE OR SULFOXIMINE OR PHOSPHINOTHRICIN OR G-
                LUTAMINE)
S4       2      S3 AND ANTI(3N)BACTER?
? s s3 and (glutamine()synth?)
Processing
Processing
Processed 10 of 10 files ...
Completed processing all files
                82 S3
                154190 GLUTAMINE
                5910402 SYNTH?
                32944 GLUTAMINE(W)SYNTH?
S5       74     S3 AND (GLUTAMINE()SYNTH?)
? s s5 and py<2002
Processing
Processing
Processing
Processing
Processed 10 of 10 files ...
Completed processing all files
                74 S5
                77298337 PY<2002
S6       39     S5 AND PY<2002

```

```

? rd
>>>Record 440:13075717 incomplete bibliographic data - record retained in RD
set
>>>Record 440:11242977 incomplete bibliographic data - record retained in RD
set
>>>Record 440:10551256 incomplete bibliographic data - record retained in RD
set
>>>Record 440:8796867 incomplete bibliographic data - record retained in RD
set
>>>Record 440:8141401 incomplete bibliographic data - record retained in RD
set
>>>Record 440:5801034 incomplete bibliographic data - record retained in RD
set

```

```

S7       13     RD (unique items)
? t s7/3,k/all

```

```

7/3,K/1      (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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```

0013332249 BIOSIS NO.: 200100504088

High extracellular levels of Mycobacterium tuberculosis glutamine synthetase and superoxide dismutase in actively growing cultures are due to high expression and extracellular stability rather than to a protein-specific export mechanism

AUTHOR: Tullius Michael V; Harth Gunter; Horwitz Marcus A (Reprint
AUTHOR ADDRESS: Division of Infectious Diseases, Department of Medicine,
School of Medicine, UCLA, 10833 Le Conte Ave., CHS 37-121, Los Angeles,
CA, 90095-1688, USA**USA

JOURNAL: Infection and Immunity 69 (10): p6348-6363 October, 2001 2001

MEDIUM: print

ISSN: 0019-9567

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

High extracellular levels of *Mycobacterium tuberculosis* glutamine synthetase and superoxide dismutase in actively growing cultures are due to high expression and extracellular stability...

...AUTHOR: Horwitz Marcus A
2001

ABSTRACT: Glutamine synthetase (GS) and superoxide dismutase (SOD), large multimeric enzymes that are thought to play important roles in the pathogenicity of *Mycobacterium tuberculosis*, are among the bacterium's major culture filtrate proteins in actively growing cultures. Although...

...of export, we cloned the homologous genes (glnA1 and sodA) from the rapid-growing, nonpathogenic *Mycobacterium smegmatis*, generated glnA1 and sodA mutants of *M. smegmatis* by allelic exchange, and quantitated expression...

...REGISTRY NUMBERS: glutamine synthetase ;
DESCRIPTORS:

...ORGANISMS: *Mycobacterium smegmatis* (Mycobacteriaceae...

... *Mycobacterium tuberculosis* (Mycobacteriaceae

CHEMICALS & BIOCHEMICALS: glutamine synthetase {GS...

GENE NAME: *Mycobacterium tuberculosis* glnA1 gene (Mycobacteriaceae...

... *Mycobacterium tuberculosis* sodA gene (Mycobacteriaceae

7/3,K/2 (Item 2 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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0012384759 BIOSIS NO.: 200000103072

Treatment of *Mycobacterium tuberculosis* with antisense oligonucleotides to glutamine synthetase mRNA inhibits glutamine synthetase activity, formation of the poly-L-glutamate/ glutamine cell wall structure, and bacterial replication

AUTHOR: Harth Gunter; Zamecnik Paul C; Tang Jin-Yan; Tabatadze David; Horwitz Marcus A (Reprint

AUTHOR ADDRESS: Division of Infectious Diseases, Department of Medicine, School of Medicine, University of California, 10833 Le Conte Avenue, 37-121 CHS, Los Angeles, CA, 90095, USA**USA

JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 97 (1): p418-423 Jan. 4, 2000 2000

MEDIUM: print

ISSN: 0027-8424

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

Treatment of *Mycobacterium tuberculosis* with antisense oligonucleotides to glutamine synthetase mRNA inhibits glutamine synthetase activity, formation of the poly-L-glutamate/ glutamine cell wall structure, and bacterial replication

...AUTHOR: Horwitz Marcus A
2000

ABSTRACT: New antibiotics to combat the emerging pandemic of drug-resistant strains of *Mycobacterium tuberculosis* are urgently needed. We have investigated the effects on *M. tuberculosis* of phosphorothioate-modified antisense oligodeoxyribonucleotides (PS-ODNs) against the mRNA of

glutamine synthetase , an enzyme whose export is associated with pathogenicity and with the formation of a poly-L-glutamate/ **glutamine** cell wall structure. Treatment of virulent *M. tuberculosis* with 10 μ M antisense PS-ODNs reduced **glutamine synthetase** activity and expression by 25-50% depending on whether one, two, or three different PS ...

...specific target sites on the mRNA. Treatment with PS-ODNs of a recombinant strain of *Mycobacterium smegmatis* expressing *M. tuberculosis* **glutamine synthetase** selectively inhibited the recombinant enzyme but not the endogenous enzyme for which the mRNA transcript...

...*M. tuberculosis* with the antisense PS-ODNs also reduced the amount of poly-L-glutamate/ **glutamine** in the cell wall by 24%. Finally, treatment with antisense PS-ODNs reduced *M. tuberculosis*...

...ODNs) but had no effect on the growth of *M. smegmatis*, which does not export **glutamine synthetase** nor possess the poly-L-glutamate/ **glutamine** (P-L-glx) cell wall structure. The experiments indicate that the antisense PS-ODNs enter...

...REGISTRY NUMBERS: **glutamine synthetase**

DESCRIPTORS:

ORGANISMS: *Mycobacterium smegmatis* (Mycobacteriaceae...

... *Mycobacterium tuberculosis* (Mycobacteriaceae

CHEMICALS & BIOCHEMICALS: **glutamine synthetase** --...

... **glutamine synthetase** mRNA...

...poly-L-glutamate/ **glutamine** --

7/3,K/3 (Item 3 from file: 5)

DIALOG(R)File 5: Biosis Previews(R)

(c) 2006 The Thomson Corporation. All rts. reserv.

0012014555 BIOSIS NO.: 199900274215

An inhibitor of exported *Mycobacterium tuberculosis* **glutamine synthetase** selectively blocks the growth of pathogenic mycobacteria in axenic culture and in human monocytes: Extracellular proteins as potential novel drug targets

AUTHOR: Harth Gunter; Horwitz Marcus A (Reprint

AUTHOR ADDRESS: Department of Medicine, 37-121 CHS, School of Medicine, University of California at Los Angeles, 10833 Le Conte Ave., Los Angeles, CA, 90095, USA**USA

JOURNAL: Journal of Experimental Medicine 189 (9): p1425-1435 May 3, 1999 1999

MEDIUM: print

ISSN: 0022-1007

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

An inhibitor of exported *Mycobacterium tuberculosis* **glutamine synthetase** selectively blocks the growth of pathogenic mycobacteria in axenic culture and in human monocytes: Extracellular...

...AUTHOR: Horwitz Marcus A

1999

ABSTRACT: *Mycobacterium tuberculosis* and other pathogenic mycobacteria export abundant quantities of proteins into their extracellular milieu when growing either axenically or within phagosomes of host cells. One major extracellular protein, the enzyme **glutamine synthetase**, is of particular interest because of its link to pathogenicity. Pathogenic mycobacteria, but not nonpathogenic...

...Interestingly, export of the enzyme is associated with the presence of a poly-L-glutamate/ **glutamine** structure in the mycobacterial cell wall. In this study, we investigated the influence of **glutamine synthetase** inhibitors on the growth of pathogenic and nonpathogenic mycobacteria and on the poly-L-glutamate/ **glutamine** cell wall structure. The inhibitor L-methionine -S- sulfoximine rapidly inactivated purified *M. tuberculosis* **glutamine synthetase**, which was 100-fold more sensitive to this inhibitor than a representative mammalian **glutamine synthetase**. Added to cultures of pathogenic mycobacteria, L-methionine -S- sulfoximine rapidly inhibited extracellular **glutamine synthetase** in a concentration-dependent manner but had only a minimal effect on cellular **glutamine synthetase**, a finding consistent with failure of the drug to cross the mycobacterial cell wall. Remarkably, the inhibitor selectively blocked the growth of pathogenic mycobacteria, all of which release **glutamine synthetase** extracellularly, but had no effect on nonpathogenic mycobacteria or nonmycobacterial microorganisms, none of which release **glutamine synthetase** extracellularly. The inhibitor was also bacteriostatic for *M. tuberculosis* in human mononuclear phagocytes (THP-1...

...perhaps underlying its bacteriostatic effect, the inhibitor markedly reduced the amount of poly-L-glutamate/ **glutamine** cell wall structure in *M. tuberculosis*. Although it is possible that **glutamine synthetase** inhibitors interact with additional extracellular proteins or structures, our findings support the concept that extracellular...

...REGISTRY NUMBERS: **glutamine** ; ...

... **glutamine** ; ...

... **glutamine synthetase** ; ...

...poly-L- **glutamine**

DESCRIPTORS:

...ORGANISMS: *Mycobacterium tuberculosis* (Mycobacteriaceae

CHEMICALS & BIOCHEMICALS: ... **glutamine** ; ...

... **glutamine synthetase** ; ...

...poly-L- **glutamine**

7/3,K/4 (Item 4 from file: 5)

DIALOG(R)File '5:Biosis Previews(R)

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0011125678 BIOSIS NO.: 199799759738

Expression and efficient export of enzymatically active *Mycobacterium tuberculosis* glutamine synthetase in *Mycobacterium smegmatis* and evidence that the information for export is contained within the protein

AUTHOR: Harth Gunter; Horwitz Marcus A (Reprint

AUTHOR ADDRESS: Div. Infect. Dis., Dep. Med., 37-121 CHS, Sch. Med., UCLA, 10883 Le Conte Ave., Los Angeles, CA 90095, USA**USA

JOURNAL: Journal of Biological Chemistry 272 (36): p22728-22735 1997 1997

ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

Expression and efficient export of enzymatically active *Mycobacterium tuberculosis* glutamine synthetase in *Mycobacterium smegmatis* and evidence that the information for export is contained within the protein
...AUTHOR: Horwitz Marcus A
1997

ABSTRACT: We have investigated the expression and extracellular release of active, recombinant *Mycobacterium tuberculosis* glutamine synthetase (EC 6.3.1.2), an enzyme that is a potentially important determinant of *M. tuberculosis* infection and whose extracellular release is correlated with pathogenicity. The *M. tuberculosis* glutamine synthetase gene encodes a polypeptide of 478 amino acids; 12 such subunits comprise the active enzyme. Northern blot, nuclease S1, and primer extension analyses revealed glutamine synthetase specific transcripts of approx 1,550 and 1,650 nucleotides produced under low and high nitrogen conditions, respectively. Expression of recombinant *M. tuberculosis* glutamine synthetase in *Escherichia coli* YMC21E, a glutamine synthetase deletion mutant, led to transcomplementation of the mutant but not to release of active enzyme. Expression in *Mycobacterium smegmatis* 1-2c, from the gene's own promoter, resulted in the release of gt 95% of all recombinant enzyme. No hybrid molecules containing *M. tuberculosis* and *M. smegmatis* glutamine synthetase subunits were detected. Native and recombinant exported and intracellular glutamine synthetase molecules were indistinguishable from one another by mass, N-terminal amino acid sequence, antibody reactivity, and enzymatic activity. Since *M. tuberculosis* glutamine synthetase is similar to other, strictly intracellular, bacterial glutamine synthetases and the DNA sequence upstream of the structural gene does not encode a leader peptide...

...REGISTRY NUMBERS: GLUTAMINE SYNTHETASE ;

DESCRIPTORS:

...ORGANISMS: *Mycobacterium smegmatis* (Mycobacteriaceae...)

... *Mycobacterium tuberculosis* (Mycobacteriaceae)

CHEMICALS & BIOCHEMICALS: GLUTAMINE SYNTHETASE ;

MISCELLANEOUS TERMS: ... GLUTAMINE SYNTHETASE ; ...

... GLUTAMINE SYNTHETASE GENE

7/3,K/5 (Item 5 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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0009694391 BIOSIS NO.: 199598162224

Characterization of *Mycobacterium tuberculosis* glutamine synthetase

AUTHOR: Harth Gunter; Clemens Daniel L; Horwitz Marcus A

AUTHOR ADDRESS: Dep. Med., Sch. Med., Univ. Calif., Los Angeles, CA 90024, USA**USA

JOURNAL: Journal of Cellular Biochemistry Supplement 0 (19B): p68 1995
1995

CONFERENCE/MEETING: Keystone Symposium on Molecular Mechanisms in Tuberculosis Tamarron, Colorado, USA February 19-25, 1995; 19950219

ISSN: 0733-1959

DOCUMENT TYPE: Meeting; Meeting Abstract; Meeting Poster

RECORD TYPE: Citation

LANGUAGE: English

Characterization of Mycobacterium tuberculosis glutamine synthetase

...AUTHOR: Horwitz Marcus A

1995

...REGISTRY NUMBERS: GLUTAMINE SYNTHETASE ; ...

... GLUTAMINE ; ...

... GLUTAMINE

DESCRIPTORS:

ORGANISMS: Mycobacterium tuberculosis (Mycobacteriaceae)

CHEMICALS & BIOCHEMICALS: GLUTAMINE SYNTHETASE ; ...

... GLUTAMINE

MISCELLANEOUS TERMS: ...EXTRACELLULAR GLUTAMINE SYNTHESIS ;

7/3,K/6 (Item 1 from file: 73)

DIALOG(R) File: 73:EMBASE

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05888998 EMBASE No: 1994302190

Glutamine synthetase of Mycobacterium tuberculosis: Extracellular release and characterization of its enzymatic activity

Harth G.; Clemens D.L.; Horwitz M.A.

Center for the Health Sciences, School of Medicine, University of California, 10833 Le Conte Avenue, Los Angeles, CA 90024 United States
Proceedings of the National Academy of Sciences of the United States of America (PROC. NATL. ACAD. SCI. U. S. A.) (United States) 1994, 91/20 (9342-9346)

CODEN: PNASA ISSN: 0027-8424

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Glutamine synthetase of Mycobacterium tuberculosis: Extracellular release and characterization of its enzymatic activity

Harth G.; Clemens D.L.; Horwitz M.A.

We have investigated the activity and extracellular release of **glutamine synthetase** (L-glutamate:ammonia ligase (ADP-forming), EC 6.3.1.2) of **Mycobacterium tuberculosis**. The purified, homogeneous M. tuberculosis **glutamine synthetase** appears to consist of 12 most likely identical subunits of M(r) 58,000, arranged in two superimposed hexagons. In the catalysis of L- **glutamine**, the enzyme has an apparent K(m) for L-glutamate of approx. eq.3 mM...

...releases the enzyme into its phagosome in infected human monocytes. Two potentially important roles for **glutamine synthetase** in the pathogenesis of M. tuberculosis infection are (i) the synthesis of L- **glutamine**, a major component of the cell wall of pathogenic but not nonpathogenic mycobacteria, and (ii)...

DRUG DESCRIPTORS:

*glutamate ammonia ligase--endogenous compound--ec; * **glutamine** --endogenous compound--ec

MEDICAL DESCRIPTORS:

*enzyme activity; *enzyme release; * **mycobacterium tuberculosis**

...CAS REGISTRY NO.: 6899-04-3 (**glutamine**)

1994

7/3,K/7 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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07443946 Genuine Article#: 166KQ No. References: 28
Title: Export of recombinant *Mycobacterium tuberculosis* superoxide
dismutase is dependent upon both information in the protein and
mycobacterial export machinery - A model for studying export of
leaderless proteins by pathogenic mycobacteria
Author(s): Harth G; Horwitz MA (REPRINT)
Corporate Source: UNIV CALIF LOS ANGELES, SCH MED, DEPT MED, DIV INFECT DIS,
10833 LE CONTE AVE/LOS ANGELES//CA/90095 (REPRINT); UNIV CALIF LOS
ANGELES, SCH MED, DEPT MED, DIV INFECT DIS/LOS ANGELES//CA/90095
Journal: JOURNAL OF BIOLOGICAL CHEMISTRY, 1999 , V274, N7 (FEB 12), P
4281-4292
ISSN: 0021-9258 Publication date: 19990212
Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE
PIKE, BETHESDA, MD 20814
Language: English Document Type: ARTICLE (ABSTRACT AVAILABLE)

Title: Export of recombinant *Mycobacterium tuberculosis* superoxide
dismutase is dependent upon both information in the protein and
mycobacterial export machinery...
Author(s): Harth G; Horwitz MA (REPRINT)
, 1999
...Abstract: extracellular release of enzymatically active superoxide
dismutase, one of the 10 major extracellular proteins of *Mycobacterium*
tuberculosis, both in its native host and in the heterologous host
Mycobacterium *smegmatis*, We found that the M, tuberculosis superoxide
dismutase gene, encoding a leaderless polypeptide of...
...at a B-fold increased level under conditions of hydrogen peroxide
stress. The highly pathogenic *mycobacterium* *M. tuberculosis* expresses
93-fold more superoxide dismutase than the nonpathogenic *mycobacterium*
M. smegmatis, and it exports a much higher proportion of expressed
enzyme (76 versus 21...
...Identifiers--ESCHERICHIA-COLI; GLUTAMINE - SYNTHETASE ; EXPRESSION;
GENE; IDENTIFICATION; PHAGOCYTOSIS; RECEPTORS; SEQUENCE; ANTIGEN;
RELEASE

7/3,K/8 (Item 1 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)
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13075717
ISSN: 0019-9567
JOURNAL: INFECTION AND IMMUNITY , 2001
(TABLE OF CONTENTS RECORD)
(The Complete Table of Contents now Available in Format 19)

, 2001

...101 REFERENCES

Section Heading: MOLECULAR PATHOGENESIS

P. 5967-5973. Silencing of oxidative stress response in *Mycobacterium*
tuberculosis: Expression patterns of *ahpC* in virulent and avirulent
strains and effect of *ahpC* inactivation...MD/20814. English.

ARTICLE. 64 REFERENCES. ABSTRACT AVAILABLE

- P. 6348-6363. High extracellular levels of **Mycobacterium tuberculosis glutamine synthetase** and superoxide dismutase in actively growing cultures are due to high expression and extracellular stability rather than to a protein-specific export mechanism. Tullius MV; Harth G; Horwitz MA. Univ Calif Los Angeles, Div Infect Dis, CHS 37-121, 10833 Le Conte Ave...02115. English. ARTICLE. 29 REFERENCES. ABSTRACT AVAILABLE
- P. 6156-6164. Enhancement of innate immunity against **Mycobacterium avium** infection by immunostimulatory DNA is mediated by indoleamine 2,3-dioxygenase. Hayashi T; Rao...inhibitory molecules down-regulate the cytolytic activity of human CD4(+) T-cell clones specific for **Mycobacterium tuberculosis**. Merlo A; Saverino D; Tenca C; Grossi CE; Bruno S; Ciccone E. Univ Genoa...

7/3,K/9 (Item 2 from file: 440)

DIALOG(R) File 440:Current Contents Search(R)
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11242977

ISSN: 0027-8424

JOURNAL: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA , 2000

(TABLE OF CONTENTS RECORD)

(The Complete Table of Contents now Available in Format 19)

, 2000

...College Pk//MD/20742. English. ARTICLE. 47 REFERENCES. ABSTRACT AVAILABLE

- P. 418-423. Treatment of **Mycobacterium tuberculosis** with antisense oligonucleotides to **glutamine synthetase** mRNA inhibits **glutamine synthetase** activity, formation of the poly-L-glutamate/**glutamine** cell wall structure, and bacterial replication. Harth G; Zamecnik PC; Tang JY; Tabatadze D; Horwitz MA. Univ Calif Los Angeles, Sch Med, 37-121 CHS, 10833 Conte Ave/Los Angeles...

7/3,K/10 (Item 3 from file: 440)

DIALOG(R) File 440:Current Contents Search(R)
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10551256

ISSN: 0022-1007

JOURNAL: JOURNAL OF EXPERIMENTAL MEDICINE , 1999

(TABLE OF CONTENTS RECORD)

(The Complete Table of Contents now Available in Format 19)

, 1999

...South Africa/. English. ARTICLE. 41 REFERENCES. ABSTRACT AVAILABLE

- P. 1425-1435. An inhibitor of exported **Mycobacterium tuberculosis glutamine synthetase** selectively blocks the growth of pathogenic mycobacteria in axenic culture and in human monocytes: Extracellular

proteins as potential novel drug targets. Harth G; Horwitz MA.
Univ Calif Los Angeles, Dept Med, 37-121 CHS, 10833 Le Conte Ave/Los
...

7/3,K/11 (Item 4 from file: 440)
DIALOG(R) File 440:Current Contents Search(R)
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08796867
ISSN: 0021-9258
JOURNAL: JOURNAL OF BIOLOGICAL CHEMISTRY , 1997
(TABLE OF CONTENTS RECORD)
(The Complete Table of Contents now Available in Format 19)

, 1997

....P. 22728-22735. Expression and efficient export of enzymatically active **Mycobacterium tuberculosis glutamine synthetase** in **Mycobacterium smegmatis** and evidence that the information for export is contained within the protein. Harth G; Horwitz MA. UNIV CALIF LOS ANGELES, SCH MED, DEPT MED, DIV INFECT DIS, 10833 LE CONTE...P. 22875-22883. Characterization of rat liver-specific **methionine adenosyltransferase** gene promoter - Role of distal upstream cis-acting elements in the regulation of the...

7/3,K/12 (Item 5 from file: 440)
DIALOG(R) File 440:Current Contents Search(R)
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08141401
ISSN: 0019-9567
JOURNAL: INFECTION AND IMMUNITY , 1997
(TABLE OF CONTENTS RECORD)
(The Complete Table of Contents now Available in Format 19)

, 1997

...P. 387-394. Analysis of culture filtrate and cell wall-associated antigens of **Mycobacterium paratuberculosis** with monoclonal antibodies. Mutharia LM; Moreno W; Raymond M. UNIV GUELPH, DEPT MICROBIOL/GUELPH...P. 587-596. Simultaneous prevention of **glutamine synthesis** and high-affinity transport attenuates *Salmonella typhimurium* virulence. Klose KE; Mekalanos JJ. HARVARD UNIV, SCH...P. 676-684. Induction of cytotoxic T-Cell responses against culture filtrate antigens in **Mycobacterium bovis bacillus Calmette-Guerin**-infected mice. Denis O; Lozes E; Huygen K. INST PASTEUR, LAB...

P. 692-698. Effects of **Mycobacterium tuberculosis** on the bioelectric properties of the alveolar epithelium. Zhang M; Kim KJ; Iyer DP. 767-773. **Mycobacterium marinum** causes both long-term subclinical infection and acute disease in the leopard frog (*Rana*...insights into the genetics, biochemistry, and immunocytochemistry of the 30-kilodalton major extracellular protein of **Mycobacterium tuberculosis** (vol 64, pg 3041, 1996). Harth G; Lee BY; Wang J; Clemens DL; Horwitz MA. UNIV CALIF LOS ANGELES, SCH MED, DEPT MED, DIV INFECT DIS/LOS ANGELES//CA...

7/3,K/13 (Item 6 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)
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05801034
ISSN: 0027-8424
JOURNAL: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED
STATES OF AMERICA , 1994
(TABLE OF CONTENTS RECORD)
(The Complete Table of Contents now Available in Format 19)

, 1994

...P. 9342-9346. **GLUTAMINE SYNTHETASE OF MYCOBACTERIUM**
TUBERCULOSIS - EXTRACELLULAR RELEASE AND CHARACTERIZATION OF ITS
ENZYMATIC ACTIVITY. HARTH G; CLEMENS DL; HORWITZ MA. UNIV
CALIF LOS ANGELES, SCH MED, CTR HLTH SCI 37121, DEPT MED, DIV INFECT...

? ds

| Set | Items | Description |
|--------------------|---------|--|
| S1 | 2529 | AU=((HORWITZ, M?) OR (HORWITZ M?)) |
| S2 | 443 | S1 AND MYCOBACTERIUM |
| S3 | 82 | S2 AND (METHIONINE OR SULFOXIMINE OR PHOSPHINOTHRICIN OR G- LUTAMINE) |
| S4 | 2 | S3 AND ANTI(3N)BACTER? |
| S5 | 74 | S3 AND (GLUTAMINE())SYNTH?) |
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| S7 | 13 | RD (unique items) |
| ? s s5 and py=2002 | | |
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| S8 | 6 | S5 AND PY=2002 |
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| S9 | 1 | RD (unique items) |
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9/3,K/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0014097197 BIOSIS NO.: 200300055916
**Targeting the Mycobacterium tuberculosis 30/32-kDa mycolyl transferase
complex as a therapeutic strategy against tuberculosis: Proof of
principle by using antisense technology.**
AUTHOR: Harth Gunter; Horwitz Marcus A (Reprint); Tabatadze David; Zamecnik
Paul C
AUTHOR ADDRESS: Division of Infectious Diseases, Department of Medicine,
University of California, 10833 Le Conte Avenue, 37-121 Center for Health
Sciences, School of Medicine, Los Angeles, CA, 90095, USA**USA
AUTHOR E-MAIL ADDRESS: mhorwitz@mednet.ucla.edu
JOURNAL: Proceedings of the National Academy of Sciences of the United
States of America 99 (24): p15614-15619 November 26, 2002 2002
MEDIUM: print
ISSN: 0027-8424 (ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

2002

? logoff

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18jul06 14:37:19 User291213 Session D65.3
  $17.15    2.907 DialUnits File5
    $12.30   6 Type(s) in Format  3
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  $20.77    1.855 DialUnits File73
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    $3.10   1 Types
$23.87 Estimated cost File73
  $3.81     0.930 DialUnits File35
$3.81 Estimated cost File35
  $48.18    2.053 DialUnits File34
    $6.82   1 Type(s) in Format  3
    $6.82   1 Types
$55.00 Estimated cost File34
  $11.23    2.496 DialUnits File144
$11.23 Estimated cost File144
  $8.64     2.541 DialUnits File155
    $0.44   2 Type(s) in Format  3
    $0.00   2 Type(s) in Format  8
    $0.44   4 Types
$9.08 Estimated cost File155
  $6.20     1.000 DialUnits File24
$6.20 Estimated cost File24
  $63.01    2.585 DialUnits File440
    $39.84   6 Type(s) in Format  3
    $39.84   6 Types
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  $16.22    0.727 DialUnits File357
$16.22 Estimated cost File357
  $2.72     0.605 DialUnits File162
$2.72 Estimated cost File162
  OneSearch, 10 files, 17.699 DialUnits FileOS
$3.46 TELNET
$263.89 Estimated cost this search
$278.33 Estimated total session cost 22.115 DialUnits
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Logoff: level 05.12.03 D 14:37:19

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NEW FILES RELEASED

***Trademarkscan - South Korea (File 655)

***Regulatory Affairs Journals (File 183)

***Index Chemicus (File 302)

***Inspec (File 202)

RESUMED UPDATING

***File 141, Reader's Guide Abstracts

RELOADS COMPLETED

***File 516, D&B--Dun's Market Identifiers

***File 523, D&B European Dun's Market Identifiers

***File 531, American Business Directory

*** MEDLINE has been reloaded with the 2006 MeSH (Files 154 & 155)

*** The 2005 reload of the CLAIMS files (Files 340, 341, 942)

is now available online.

DATABASES REMOVED

***File 196, FINDEX

***File 468, Public Opinion Online (POLL)

Chemical Structure Searching now available in Prous Science Drug Data Report (F452), Prous Science Drugs of the Future (F453), IMS R&D Focus (F445/955), Pharmaprojects (F128/928), Beilstein Facts (F390), Derwent Chemistry Resource (F355) and Index Chemicus (File 302).

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? sf all

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\$0.83 0.237 DialUnits File1

\$0.83 Estimated cost File1

\$0.14 TELNET

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\$0.97 Estimated total session cost 0.237 DialUnits

File 411:DIALINDEX(R)

DIALINDEX(R)

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s au=((horwitz, M?) or (Horwitz M?))

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? s au=((horwitz, M?) or (Horwitz M?))

Your SELECT statement is:

s au=((horwitz, M?) or (Horwitz M?))

| Items | File |
|-------|------|
|-------|------|

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| 7 | 1: ERIC_1966-2006/June |
| 7 | 2: INSPEC_1898-2006/Jul W2 |
| 476 | 5: Biosis Previews(R)_1969-2006/Jul W2 |
| 9 | 6: NTIS_1964-2006/Jul W2 |
| 44 | 7: Social SciSearch(R)_1972-2006/Jul W2 |
| 8 | 8: Ei Compendex(R)_1970-2006/Jul W2 |
| 19 | 10: AGRICOLA_70-2006/May |
| 22 | 11: PsycINFO(R)_1887-2006/Apr W4 |
| 7 | 15: ABI/Inform(R)_1971-2006/Jul 18 |
| 1 | 16: Gale Group PROMT(R)_1990-2006/Jul 17 |
| 1 | 18: Gale Group F&S Index(R)_1988-2006/Jul 17 |
| 1 | 21: NCJRS_1972-2006/Jun |
| 189 | 24: CSA Life Sciences Abstracts_1966-2006/May |
| 329 | 34: SciSearch(R) Cited Ref Sci_1990-2006/Jul W2 |
| 10 | 35: Dissertation Abs Online_1861-2006/Jun |
| 19 | 38: America:History & Life_1963-2005/Q3 |
| 3 | 47: Gale Group Magazine DB(TM)_1959-2006/Jul 14 |
| 22 | 50: CAB Abstracts_1972-2006/Jun |
| 6 | 51: Food Sci.&Tech.Abs_1969-2006/Jul W3 |
| 5 | 53: FOODLINE(R): Science_1972-2006/Jul 18 |
| 1 | 61: Civil Engineering Abstracts._1966-2006/Jul |
| 1 | 62: SPIN(R)_1975-2006/Apr W3 |
| 2 | 63: Transport Res(TRIS)_1970-2006/Jun |
| Examined 50 | files |
| 16 | 65: Inside Conferences_1993-2006/Jul 18 |
| 1 | 66: GPO Mon. Cat._1978-2006/Jul |
| 170 | 71: ELSEVIER BIOBASE_1994-2006/Jul W3 |
| 321 | 73: EMBASE_1974-2006/Jul 18 |
| 39 | 88: Gale Group Business A.R.T.S._1976-2006/Jul 06 |
| 1 | 89: GeoRef_1785-2006/Jul B1 |
| 3 | 91: MANTIS(TM)_1880-2006/Jan |
| 21 | 98: General Sci Abs_1984-2005/Jan |
| 1 | 99: Wilson Appl. Sci & Tech Abs_1983-2006/Jun |
| 7 | 103: Energy SciTec_1974-2006/May B2 |
| 1 | 111: TGG Natl.Newspaper Index(SM)_1979-2006/Jul 05 |
| 92 | 120: U.S. Copyrights_1978-2006/Jul 11 |
| Examined 100 | files |
| 3 | 136: BioEngineering Abstracts_1966-2006/May |
| 45 | 137: Book Review Index_1969-2004/May |
| 3 | 139: EconLit_1969-2006/Jul |

5 141: Readers Guide_1983-2006/Jun
 4 142: Social Sciences Abstracts_1983-2006/Jun
 55 143: Biol. & Agric. Index_1983-2006/Jun
 266 144: Pascal_1973-2006/Jun W4
 4 148: Gale Group Trade & Industry DB_1976-2006/Jul 14
 10 149: TGG Health&Wellness DB(SM)_1976-2006/Jun W4
 37 150: Gale Group Legal Res Index(TM)_1980-2006/Jul 13
 386 155: MEDLINE(R)_1950-2006/Jul 17
 61 156: ToxFile_1965-2006/Jul W2
 90 159: Cancerlit_1975-2002/Oct
 44 162: Global Health_1983-2006/Jun
 1 163: Ageline(R)_1965-2006/Jun
 4 172: EMBASE Alert_2006/Jul 18
 2 173: Adis Clinical Trials Insight_2000-2006/Jul W1
 1 174: Pharm-line(R)_1978-2002/Dec W3
 3 203: AGRIS_1974-2006/Mar
 2 205: ONTAP(R) BIOSIS Previews(R)_
 Examined 150 files
 3 211: Gale Group Newsearch(TM)_2006/Jul 14
 1 240: PAPERCHEM_1967-2006/Jul W3
 2 254: ONTAP(R) MEDLINE(R)_2005
 10 266: FEDRIP_2005/Dec
 1 272: ONTAP(R) EMBASE
 1 280: ONTAP Derwent World Patents Index
 Examined 200 files
 2 285: BioBusiness(R)_1985-1998/Aug W1
 2 315: ChemEng & Biotec Abs_1970-2006/Jun
 35 340: CLAIMS(R)/US Patent_1950-06/Jul 13
 28 342: Derwent Patents Citation Indx_1978-05/200643
 25 345: Inpadoc/Fam. & Legal Stat_1968-2006/UD=200628
 1 347: JAPIO Dec 1976-2005/Dec(Updated 060404)
 15 348: EUROPEAN PATENTS_1978-2006/ 200628
 17 349: PCT FULLTEXT_1979-2006/UB=20060713,UT=20060706
 26 357: Derwent Biotech Res._1982-2006/Jul W2
 2 358: Current BioTech Abs_1983-2006/Jan
 1 370: Science_1996-1999/Jul W3
 9 373: Adis Clinical Trials Insight_1982-June 2000
 12 376: Derwent Drug File_1964-1982
 Examined 250 files
 43 377: Derwent Drug File_1983-2006/Jun W3
 288 399: CA SEARCH(R)_1967-2006/UD=14504
 117 420: UnCover_1988-2001/May 31
 25 426: LCMARC-Books_1968-2006/Jul W3
 5 430: British Books in Print_2006/Jul W3
 125 434: SciSearch(R) Cited Ref_Sci_1974-1989/Dec
 2 436: Humanities Abs_1984-2004/Dec
 3 437: Education Abstracts_1983-2006/Jun
 1 438: Library Lit. & Info. Science_1984-2006/Jun
 4 439: Arts&Humanities Search(R)_1980-2006/Jul W2
 482 440: Current Contents Search(R)_1990-2006/Jul 18
 1 444: New England Journal of Med._1985-2006/Jul W1
 Examined 300 files
 7 474: New York Times Abs_1969-2006/Jul 17
 6 483: Newspaper Abs Daily_1986-2006/Jul 13
 29 484: Periodical Abs Plustext_1986-2006/Jul W2
 22 485: Accounting & Tax DB_1971-2006/Jul W2
 Examined 350 files
 3 553: Wilson Bus. Abs._1982-2006/Jul
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| NEWS | 3 FEB 27 | New STN AnaVist pricing effective March 1, 2006 |
| NEWS | 4 APR 04 | STN AnaVist \$500 visualization usage credit offered |
| NEWS | 5 MAY 10 | CA/CAPLUS enhanced with 1900-1906 U.S. patent records |
| NEWS | 6 MAY 11 | KOREAPAT updates resume |
| NEWS | 7 MAY 19 | Derwent World Patents Index to be reloaded and enhanced |
| NEWS | 8 MAY 30 | IPC 8 Rolled-up Core codes added to CA/CAPLUS and USPATFULL/USPAT2 |
| NEWS | 9 MAY 30 | The F-Term thesaurus is now available in CA/CAPLUS |
| NEWS | 10 JUN 02 | The first reclassification of IPC codes now complete in INPADOC |
| NEWS | 11 JUN 26 | TULSA/TULSA2 reloaded and enhanced with new search and and display fields |
| NEWS | 12 JUN 28 | Price changes in full-text patent databases EPFULL and PCTFULL |
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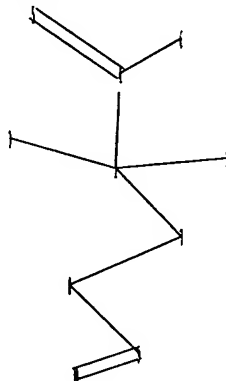
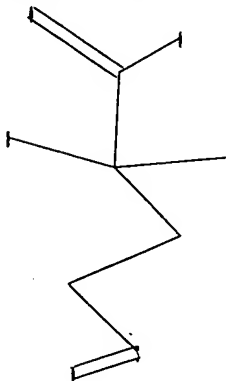
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 FILE LAST UPDATED: 17 Jul 2006 (20060717/ED)

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chain nodes :
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 chain bonds :
 1-2 1-3 1-4 1-7 4-5 4-6 7-8 8-9 9-10
 exact/norm bonds :
 1-3 4-5 4-6 8-9 9-10
 exact bonds :
 1-2 1-4 1-7 7-8

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 10:CLASS

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PROJECTED ITERATIONS: 33 TO 447
PROJECTED ANSWERS: 4 TO 200

L2 4 SEA SSS SAM L1

L3 5 L2

=> DIS L3 1 SAM IBIB IABS
THE ESTIMATED COST FOR THIS REQUEST IS 3.07 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L3 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
CC 80-4 (Organic Analytical Chemistry)
TI Gas chromatographic separation of enantiomeric sulfur compounds on
Chirasil-Val
ST sulfoxide enantiomer gas chromatog; sulfur compd enantiomer gas chromatog
IT Chromatography, gas
(for resolution of enantiomeric sulfur compds. on Chirasil-Val)
IT Resolution
(of sulfur compound enantiomers by gas chromatog. on Chirasil-Val)
IT Sulfoxides
RL: ANST (Analytical study)
(resolution of enantiomeric, gas chromatog.)
IT 4170-69-8 33577-16-1 95833-61-7 95833-62-8
RL: ANST (Analytical study); PROC (Process)
(resolution of, by gas chromatog. on Chirasil-Val)
IT 3226-66-2 7314-32-1 23631-84-7 34044-66-1 41486-92-4 50896-97-4
50896-98-5 80225-50-9 95833-63-9 95833-64-0 95833-65-1
95833-66-2 95833-67-3 95833-68-4 95833-69-5 95833-70-8
95833-71-9 95833-72-0 95833-73-1 95833-74-2
RL: ANST (Analytical study); PROC (Process)
(separation of, by gas chromatog. on Chirasil-Val)
ACCESSION NUMBER: 1985:178450 CAPLUS
DOCUMENT NUMBER: 102:178450
TITLE: Gas chromatographic separation of enantiomeric sulfur
compounds on Chirasil-Val
AUTHOR(S): Bayer, Ernst; Kuesters, Ernst; Nicholson, Graeme J.;
Frank, Hartmut
CORPORATE SOURCE: Inst. Org. Chem., Univ. Tuebingen, Tuebingen,
D-7400/1, Fed. Rep. Ger.
SOURCE: Journal of Chromatography (1985), 320(2), 393-6
CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The gas chromatog. separation of sulfoxide antipodes, including aliphatic
sulfoxides,
on quartz fused silica capillaries coated with the chiral silicone phase

Chirasil-Val is reported. The compds. were esterified before anal. A flame ionization detector and H carrier gas were used.

=> DIS L3 2 SAM IBIB IABS

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DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L3 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
 CC 34-2 (Synthesis of Amino Acids, Peptides, and Proteins)
 Section cross-reference(s): 22
 TI Chemical ionization mass spectra of L-methionine and L-methionine analogs
 ST methionine analog mass spectra; sulfone methionine mass spectra; sulfoxide
 methionine mass spectra; sulfoximine methionine mass spectra
 IT Amino acids, properties
 RL: PRP (Properties)
 (mass spectra of methionine and its sulfone and sulfoxide and
 sulfoximines)
 IT Mass spectra
 (chemical-ionization, of methionine and its analogs)
 IT Molecular structure-property relationship
 (mass spectra, of methionine and its sulfone and sulfoxide and
 sulfoximines)
 IT 63-68-3, properties 3226-65-1 7314-32-1 15985-39-4 78867-97-7
 78867-98-8 78867-99-9 78868-00-5 78868-01-6 78868-02-7
 RL: PRP (Properties)
 (chemical ionization mass spectrum of)

ACCESSION NUMBER: 1981:515972 CAPLUS
 DOCUMENT NUMBER: 95:115972
 TITLE: Chemical ionization mass spectra of L-methionine and
 L-methionine analogs
 AUTHOR(S): Cooper, Arthur J. L.; Griffith, Owen W.; Meister,
 Alton; Field, Frank H.
 CORPORATE SOURCE: Med. Coll., Cornell Univ. Med. Coll., New York, NY,
 10021, USA
 SOURCE: Biomedical Mass Spectrometry (1981), 8(3), 95-8
 CODEN: BMSYAL; ISSN: 0306-042X
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 ABSTRACT:

The chemical ionization mass spectra of L-methionine, L-methionine sulfone,
 L-methionine (RS)-sulfoxide, L-methionine (RS)-sulfoximine, DL-ethionine
 (RS)-sulfoximine, DL-prothionine (RS)-sulfoximine, DL-buthionine
 (RS)-sulfoximine, α -methyl-L-methionine (RS)-sulfoximine,
 α -ethyl-DL-methionine were recorded. The observed fragmentation patterns
 are discussed in relation to structural and chemical properties; the sulfoximines
 show spectra unique among amino acids.

=> DIS L3 3 SAM IBIB IABS

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DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L3 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
 CC 7-3 (Enzymes)
 Section cross-reference(s): 13
 TI Inhibitors of polyamine biosynthesis. 9. Effects of S-adenosyl-L-
 methionine analogs on mammalian aminopropyltransferases in vitro and
 polyamine biosynthesis in transformed lymphocytes
 ST aminopropyltransferase interaction adenosylmethionine analog; synthase
 spermine spermidine adenosylmethionine analog; decarboxylase inhibition

- adenosylmethionine analog; DNA formation lymphocyte adenosylmethionine analog; polyamine lymphocyte adenosylmethionine analog
- IT Lymphocyte
(DNA formation by and polyamine levels in, adenosylmethionine analog effect on)
- IT Liver, composition
(adenosylmethionine decarboxylase of, adenosylmethionine analog inhibition of)
- IT Deoxyribonucleic acids
RL: FORM (Formation, nonpreparative)
(formation of, by lymphocytes, adenosylmethionine analog effect on)
- IT Prostate gland
(spermidine and spermine synthases of, adenosylmethionine analog interaction with)
- IT Brain, composition
(spermine synthase of, adenosylmethionine analog interaction with)
- IT Amines, biological studies
RL: BIOL (Biological study)
(poly-, of lymphocyte, adenosine methionine analog effect on)
- IT 74812-43-4
RL: BIOL (Biological study)
(adenosylmethionine analog interaction with, of brain and prostate gland)
- IT 37277-82-0
RL: BIOL (Biological study)
(adenosylmethionine analog interaction with, of prostate gland)
- IT 9036-20-8
RL: PROC (Process)
(inhibition of, of liver, by adenosylmethionine analog)
- IT 61102-32-7 72648-30-7 72648-32-9 72648-35-2 72648-37-4
76858-87-2 76858-88-3
RL: BIOL (Biological study)
(spermidine and spermine synthases interaction with)

ACCESSION NUMBER: 1981:170089 CAPLUS

DOCUMENT NUMBER: 94:170089

TITLE: Inhibitors of polyamine biosynthesis. 9. Effects of S-adenosyl-L-methionine analogs on mammalian aminopropyltransferases in vitro and polyamine biosynthesis in transformed lymphocytes

AUTHOR(S): Pankaskie, Marvin C.; Abdel-Monem, Mahmoud M.; Raina, Aarne; Wang, Tinchung; Foker, John E.

CORPORATE SOURCE: Dep. Med. Chem., Univ. Minnesota, Minneapolis, MN, 55455, USA

SOURCE: Journal of Medicinal Chemistry (1981), 24(5), 549-53
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

ABSTRACT:

Seven analogs of S-adenosyl-L-methionine were studied as inhibitors or substrates for mammalian spermidine synthase (SDS) and spermine synthase (SS). One of these, S-(5'-deoxy-5'-adenosyl)-(+)-1-methyl-3-(methylthio)propylamine (I), showed a unique spectrum of activities on the polyamine biosynthesis enzymes. It was an inhibitor of adenosylmethionine decarboxylase from rat liver and SS from bovine brain and rat ventral prostate. I was a substrate for the SDS from bovine brain and rat ventral prostate, but not a substrate for the SS from these same sources. At concns. of ≥ 0.2 mM, I blocked the increases in polyamine levels and in thymidine-3H incorporation induced by concanavalin A in cultured mouse lymphocytes. At approx. 0.5 mM concentration of I, the cellular polyamine levels and the rate of thymidine incorporation were similar to those of the unstimulated lymphocytes. Lower concns. of I (0.02-0.1 mM) produced a dose-dependent increase in thymidine incorporation. A dose-dependent decrease in the cellular polyamine levels was observed in the range of 0.05-0.5 mM of the inhibitor. Thus the

effects of I on transformed lymphocytes are complex and may not be solely due to the inhibition of polyamine biosynthesis by this compound

=> DIS L3 4 SAM IBIB IABS

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DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L3 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
 CC 7-3 (Enzymes)
 TI Inhibitors of polyamine biosynthesis. 8. Irreversible inhibition of
 mammalian S-adenosyl-L-methionine decarboxylase by substrate analogs
 ST adenosylmethionine decarboxylase inhibitor substrate; adenosylmethionine
 analog enzyme inhibitor
 IT Liver, composition
 (adenosylmethionine decarboxylase of, adenosylmethionine analogs
 inhibition of)
 IT Michaelis constant
 (of adenosylmethionine decarboxylase)
 IT Kinetics, enzymic
 (of inhibition, of adenosylmethionine decarboxylase)
 IT 72648-29-4
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (acid hydrolysis of)
 IT 72648-22-7
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (hydrolysis of)
 IT 9036-20-8
 RL: PROC (Process)
 (of liver, inhibition of, by adenosylmethionine analogs)
 IT 19360-96-4P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and Bucherer-Lieb reaction of)
 IT 61102-32-7P 72648-25-0P 72648-31-8P 72648-34-1P 72648-36-3P
 72648-37-4P 72648-38-5P 72671-97-7P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation and adenosylmethionine decarboxylase inhibiting activity of)
 IT 72648-21-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and hydrolysis of)
 IT 19361-15-0P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and reaction with isopropylidenesulfonyladosine)
 IT 72648-27-2P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and reaction with isopropylidenetoluenesulfonyladosine)
 IT 72648-26-1P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and reduction of)
 IT 100-53-8
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction of, with Me vinyl ketone)
 IT 29908-03-0
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction of, with adenosylmethionine decarboxylase, kinetics of)
 IT 5605-63-0
 RL: RCT (Reactant); RACT (Reactant or reagent)

(reaction of, with amino(benzylthio)methylbutanoic acid)

IT 78-94-4, reactions
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction of, with benzylmercaptan)

IT 5135-30-8
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction of, with methylalaninenitrile)

IT 693-05-0
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction of, with toluenesulfonyladenosine)

ACCESSION NUMBER: 1980:71732 CAPLUS

DOCUMENT NUMBER: 92:71732

TITLE: Inhibitors of polyamine biosynthesis. 8.
 Irreversible inhibition of mammalian
 S-adenosyl-L-methionine decarboxylase by substrate
 analogs

AUTHOR(S): Pankaskie, Marvin; Abdel-Monem, Mahmoud M.

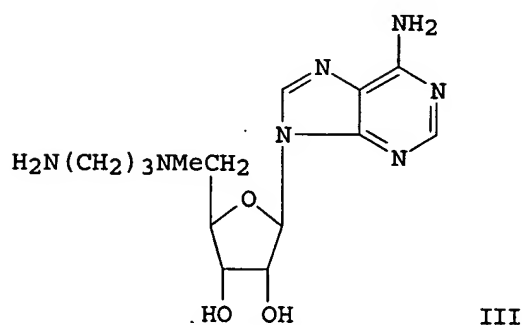
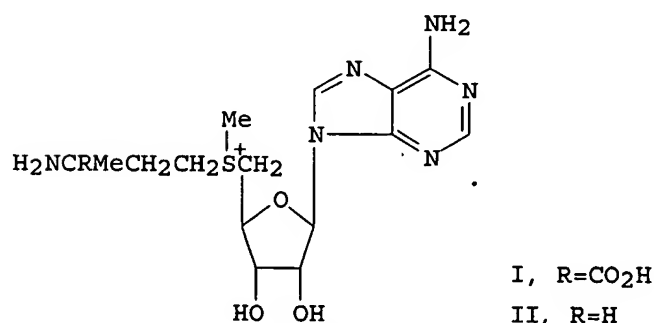
CORPORATE SOURCE: Coll. Pharm., Univ. Minnesota, Minneapolis, MN, 55455,
 USA

SOURCE: Journal of Medicinal Chemistry (1980), 23(2), 121-7
 CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

GRAPHIC IMAGE:



ABSTRACT:

Several S-adenosyl-L-methionine analogs in which the sulfonium group and the substituents of the α -C of the amino acid moiety were modified were synthesized and evaluated as inhibitors of S-adenosyl-L-methionine decarboxylase of rat liver. S-(5'-Deoxy-5'-adenosyl)-(\pm)-2-methylmethionine dihydrogen sulfate (I), the propylamine analog (II), and N-(aminopropyl)-N-methyl-5'-amino-5'-deoxyadenosine-2HCl (III) were competitive inhibitors of the enzymic decarboxylation of S-adenosyl-L-methionine by the rat liver enzyme. I

and II formed azomethine bonds with an essential CO group in the enzyme active site, and both inhibitors also caused a concentration- and time-dependent inactivation

of the enzyme. III did not form an azomethine bond with and did not cause inactivation of the enzyme. Apparently, I and II have a binding mode to the enzyme active site different than that for III.

=> DIS L3 5 SAM IBIB IABS

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L3 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
 IC C07C
 CC 23-17 (Aliphatic Compounds)
 Section cross-reference(s): 25, 27
 TI Carboxylic acids
 ST ester isocyano; arom ester isocyano; furanpropionate isocyano; addn isocyano ester alkene
 IT Esters, preparation
 RL: PREP (Preparation)
 (isocyano)
 IT Addition reaction
 (of isocyano esters with vinylic compds.)
 IT 78-94-4 94-41-7 102-96-5 107-13-1, reactions 126-98-7 3156-70-5
 4360-47-8 4786-20-3 4812-23-1 5535-48-8 33972-66-6 33972-68-8
 41409-84-1
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (addition reaction of, with isocyano alkanoates)
 IT 2999-46-4 33140-27-1
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (addition reaction of, with vinyl compds.)
 IT 38062-11-2P 38062-12-3P 38062-13-4P 38062-14-5P 38062-15-6P
 38062-16-7P 38062-17-8P 38114-92-0P 41409-70-5P 41409-74-9P
 41409-75-0P 41409-76-1P 41409-77-2P 41409-78-3P
 41409-79-4P 41409-80-7P 41409-81-8P 41409-82-9P 41409-83-0P
 41486-62-8P 41694-57-9P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)

ACCESSION NUMBER: 1973:441967 CAPLUS
 DOCUMENT NUMBER: 79:41967
 TITLE: Carboxylic acids
 INVENTOR(S): Schoellkopf, Ulrich; Stafforst, Diethard
 PATENT ASSIGNEE(S): Badische Anilin- & Soda-Fabrik AG
 SOURCE: Ger. Offen., 19 pp. Addn. to Ger. Offen. 2,043,666
 (CA 75;129661u).
 CODEN: GWXXBX
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|------------|
| DE 2147707 | A1 | 19730329 | DE 1971-2147707 | 19710924 |
| PRIORITY APPLN. INFO.: | | | DE 1971-2147707 | A 19710924 |

GRAPHIC IMAGE: For diagram(s), see printed CA Issue.

ABSTRACT:

Addition reaction of isocyanoesters CNCHRCO₂Et (R = H, Me) with acrylonitrile, vinyl sulfones, nitroalkanes, or vinyl ketones in presence of NaOMe, BuLi, or Na-EtOH gave other esters (mono- and diaddn. products). Thus, NCCHMeCO₂Et (I) and PhCH:CHCN gave NCCH₂CHPhC(NC)MeCO₂Et; I with 2,5-dihydro-3-

(methylsulfonyl)furan gave II; and CNCH₂CO₂Et with PhCH:CHNO₂ gave (O₂NCH₂CHPh) 2C(NC) CO₂Et.

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=> FIL CAPLUS

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| | ENTRY | SESSION |
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| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| CA SUBSCRIBER PRICE | 0.00 | -3.75 |

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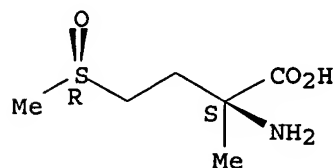
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=> DIS L3 1 HITSEQ

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 DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L3 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
 IT 95833-63-9
 RL: ANST (Analytical study); PROC (Process)
 (separation of, by gas chromatog. on Chirasil-Val)
 RN 95833-63-9 CAPLUS
 CN L-Isovaline, 4-(methylsulfinyl)-, (R)- (9CI) (CA INDEX NAME)

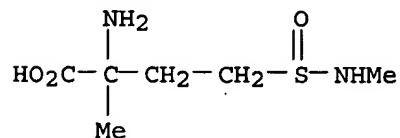
Absolute stereochemistry.



=> DIS L3 2 HITSEQ

THE ESTIMATED COST FOR THIS REQUEST IS 7.05 U.S. DOLLARS
 DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L3 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
 IT 78868-00-5
 RL: PRP (Properties)
 (chemical ionization mass spectrum of)
 RN 78868-00-5 CAPLUS
 CN Isovaline, 4-[(methylamino)sulfinyl]- (9CI) (CA INDEX NAME)



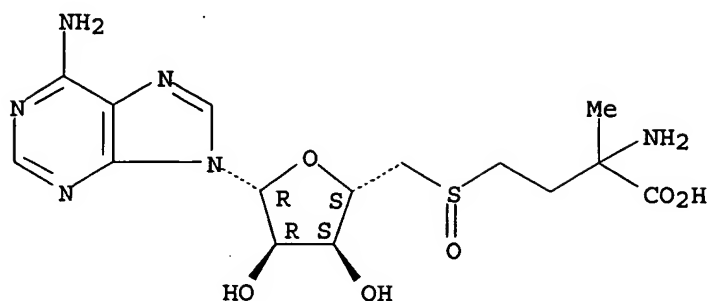
=> DIS L3 3 HITSEQ

THE ESTIMATED COST FOR THIS REQUEST IS 7.05 U.S. DOLLARS
 DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L3 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
 IT 72648-37-4
 RL: BIOL (Biological study)
 (spermidine and spermine synthases interaction with)
 RN 72648-37-4 CAPLUS
 CN Adenosine, 5'-[(3-amino-3-carboxybutyl)sulfinyl]-5'-deoxy- (9CI) (CA

INDEX NAME)

Absolute stereochemistry.



=> DIS L3 4 HITSEQ

THE ESTIMATED COST FOR THIS REQUEST IS 7.05 U.S. DOLLARS

DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L3 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

IT 72648-37-4P

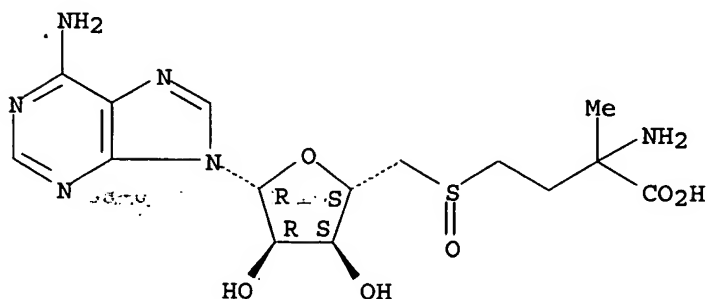
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and adenosylmethionine decarboxylase inhibiting activity of)

RN 72648-37-4 CAPLUS

CN Adenosine, 5'-[(3-amino-3-carboxybutyl)sulfinyl]-5'-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> DIS L3 5 HITSEQ

THE ESTIMATED COST FOR THIS REQUEST IS 7.05 U.S. DOLLARS

DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L3 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

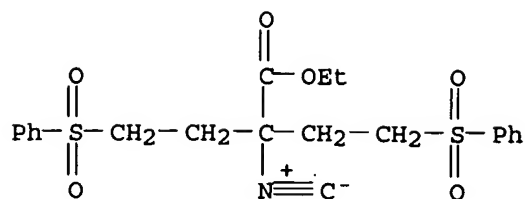
IT 41409-75-0P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of)

RN 41409-75-0 CAPLUS

CN Butanoic acid, 2-isocyano-4-(phenylsulfonyl)-2-[2-(phenylsulfonyl)ethyl]-, ethyl ester (9CI) (CA INDEX NAME)



=> FIL REGISTRY

| | | |
|--|------------------|---------------|
| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
| FULL ESTIMATED COST | 12.77 | 32.77 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
| CA SUBSCRIBER PRICE | 0.00 | -3.75 |

FILE 'REGISTRY' ENTERED AT 09:33:35 ON 18 JUL 2006
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 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 17 JUL 2006 HIGHEST RN 893880-40-5
 DICTIONARY FILE UPDATES: 17 JUL 2006 HIGHEST RN 893880-40-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=> DIS L2 1- RN SAM

'SAM' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'

The following are valid formats:

Substance information can be displayed by requesting individual fields or predefined formats. The predefined substance formats are: (RN = CAS Registry Number)

| | |
|--------|---|
| REG | - RN |
| SAM | - Index Name, MF, and structure - no RN |
| FIDE | - All substance data, except sequence data |
| IDE | - FIDE, but only 50 names |
| SQIDE | - IDE, plus sequence data |
| SQIDE3 | - Same as SQIDE, but 3-letter amino acid codes are used |
| SQD | - Protein sequence data, includes RN |
| SQD3 | - Same as SQD, but 3-letter amino acid codes are used |

SQN - Protein sequence name information, includes RN

CALC - Table of calculated properties

EPROP - Table of experimental properties

PROP - EPROP and CALC

Any CA File format may be combined with any substance format to obtain CA references citing the substance. The substance formats must be cited first. The CA File predefined formats are:

ABS -- Abstract

APPS -- Application and Priority Information

BIB -- CA Accession Number, plus Bibliographic Data

CAN -- CA Accession Number

CBIB -- CA Accession Number, plus Bibliographic Data (compressed)

IND -- Index Data

IPC -- International Patent Classification

PATS -- PI, SO

STD -- BIB, IPC, and NCL

IABS -- ABS, indented, with text labels

IBIB -- BIB, indented, with text labels

ISTD -- STD format, indented

OBIB ----- AN, plus Bibliographic Data (original)

OIBIB ----- OBIB, indented with text labels

SBIB ----- BIB, no citations

SIBIB ----- IBIB, no citations

The ALL format gives FIDE BIB ABS IND RE, plus sequence data when it is available.

The MAX format is the same as ALL.

The IALL format is the same as ALL with BIB ABS and IND indented, with text labels.

For additional information, please consult the following help messages:

HELP DFIELDS -- To see a complete list of individual display fields.

HELP FORMATS -- To see detailed descriptions of the predefined formats.

ENTER DISPLAY FORMAT (IDE):END

=> DIS L2 1- RN SAM

'SAM' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'

The following are valid formats:

Substance information can be displayed by requesting individual fields or predefined formats. The predefined substance formats are: (RN = CAS Registry Number)

REG - RN

SAM - Index Name, MF, and structure - no RN

FIDE - All substance data, except sequence data

IDE - FIDE, but only 50 names

SQIDE - IDE, plus sequence data

SQIDE3 - Same as SQIDE, but 3-letter amino acid codes are used

SQD - Protein sequence data, includes RN

SQD3 - Same as SQD, but 3-letter amino acid codes are used

SQN - Protein sequence name information, includes RN

CALC - Table of calculated properties

EPROP - Table of experimental properties
 PROP - EPROP and CALC

Any CA File format may be combined with any substance format to obtain CA references citing the substance. The substance formats must be cited first. The CA File predefined formats are:

ABS -- Abstract
 APPS -- Application and Priority Information
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 CBIB -- CA Accession Number, plus Bibliographic Data (compressed)
 IND -- Index Data
 IPC -- International Patent Classification
 PATS -- PI, SO
 STD -- BIB, IPC, and NCL

IABS -- ABS, indented, with text labels
 IBIB -- BIB, indented, with text labels
 ISTD -- STD format, indented

OBIB ----- AN, plus Bibliographic Data (original)
 OIBIB ----- OBIB, indented with text labels

SBIB ----- BIB, no citations
 SIBIB ----- IBIB, no citations

The ALL format gives FIDE BIB ABS IND RE, plus sequence data when it is available.

The MAX format is the same as ALL.

The IALL format is the same as ALL with BIB ABS and IND indented, with text labels.

For additional information, please consult the following help messages:

HELP DFIELDS -- To see a complete list of individual display fields.
 HELP FORMATS -- To see detailed descriptions of the predefined formats.
 ENTER DISPLAY FORMAT (IDE):END

=> D COST

| | | |
|--|------------|---------|
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| CONNECT CHARGES | 0.76 | 5.37 |
| NETWORK CHARGES | 0.12 | 1.08 |
| DISPLAY CHARGES | 0.00 | 27.20 |
| | ----- | ----- |
| FULL ESTIMATED COST | 0.88 | 33.65 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| CA SUBSCRIBER PRICE | 0.00 | -3.75 |

IN FILE 'REGISTRY' AT 09:34:48 ON 18 JUL 2006

=> FIL STNGUIDE

| | | |
|--|------------|---------|
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| FULL ESTIMATED COST | 0.88 | 33.65 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL |
| | ENTRY | SESSION |

229

| | | |
|---------------------|------|-------|
| CA SUBSCRIBER PRICE | 0.00 | -3.75 |
|---------------------|------|-------|

FILE 'STNGUIDE' ENTERED AT 09:35:02 ON 18 JUL 2006
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AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Jul 17, 2006 (20060717/UP).

=> logoff

ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF

LOGOFF? (Y)/N/HOLD:y

COST IN U.S. DOLLARS

FULL ESTIMATED COST

| SINCE FILE | TOTAL |
|------------|---------|
| ENTRY | SESSION |
| 0.06 | 33.71 |

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

CA SUBSCRIBER PRICE

| SINCE FILE | TOTAL |
|------------|---------|
| ENTRY | SESSION |
| 0.00 | -3.75 |

STN INTERNATIONAL LOGOFF AT 09:35:32 ON 18 JUL 2006